PURETECH

GIVING LIFE TO SCIENCE®

Giving Life to Science

PureTech Health plc ("PureTech Health", "PureTech" or "the Company") is a clinical-stage biotherapeutics company dedicated to discovering, developing and commercializing highly differentiated medicines for devastating diseases, including inflammatory, fibrotic and immunological conditions, intractable cancers, lymphatic and gastrointestinal diseases and neurological and neuropsychological disorders, among others. We discover and develop new therapies for serious diseases where limited or no treatment options currently exist for patients. The common theme underlying all of our programs has been to start with a tremendous patient need. In many cases, these programs are identified based on some previous human efficacy and clinically validated biology, which has enabled us to advance therapeutic candidates with substantially de-risked profiles and robust development rationales, resulting in differentiated treatment candidates for patients that improve on key challenges of existing therapeutics, such as poor safety, tolerability, oral bioavailability or dosing. We do this often by building upon underlying mechanisms from well-established science that have been validated in clinical testing, while applying unique innovative insight or technology that generates new medicines that can unleash the full potential of the therapeutic. We have created a broad and deep pipeline through the expertise of our experienced research and development team and our extensive network of scientists, clinicians and industry leaders. Our pipeline, which is being advanced both internally and through our Founded Entities[1], is comprised of 27 therapeutics and therapeutic candidates, including two that have received both U.S. Food and Drug Administration (FDA) clearance and European marketing authorization. All of the underlying programs and platforms that resulted in this pipeline of therapeutic candidates were initially identified or discovered and then advanced by our team through key validation points based on unique insights in immunology and drug development.

PureTech is led by a proven and seasoned management team of industry leaders with significant experience in discovering and developing important new medicines, delivering them to market and maximizing shareholder value.

Headquarters	Nasdaq	LSE
Boston, MA	PRTC	PRTC

1 Our Founded Entities are comprised of our Controlled Founded Entities and our Non-Controlled Founded Entities. References in this report to our "Controlled Founded Entities" refer to Follica, Incorporated, Vedanta Biosciences, Inc., Sonde Health, Inc. and Entrega, Inc. References in this report to our "Non-Controlled Founded Entities" refer to Gelesis Holdings, Inc., Akili Interactive Labs, Inc., Karuna Therapeutics, Inc. and Vor Bio Inc., and, for all periods prior to December 18, 2019, resTORbio, Inc. We formed each of our Founded Entities and have been involved in development efforts in varying degrees. In the case of each of our Controlled Founded Entities, we continue to maintain majority voting control. With respect to our Non-Controlled Founded Entities, we may benefit from appreciation in our minority equity investment as a shareholder of such companies.

Highlights of the Year – 2021

PureTech Level Cash and Cash Equivalents as of Year End

$418.9m[2]

2020: $349.4m
2019: $120.6m
2018: $177.7m
2017: $126.7m

Consolidated Cash and Cash Equivalents as of Year End

$465.7m[2]

Includes cash held at the PureTech level and at Controlled Founded Entities (Follica, Entrega, Vedanta, and Sonde)

2020: $403.9m
2019: $162.4m
2018: $250.9m
2017: $188.7m

Amount of funding secured for Founded Entities

$731.9m[3,4]

$709.3m (96.9%) came from third parties

2020: $247.8m
2019: $666.8m
2018: $274.0m
2017: $102.9m

Wholly Owned Programs

Our team, network and insights and expertise in immunology and therapeutic development have enabled the rapid advancement and growth of our Wholly Owned Programs[5]. Focused on immunological, fibrotic and lymphatic system disorders, our Wholly Owned Pipeline builds upon validated biologic pathways and proven pharmacology, and currently consists of seven therapeutic candidates, including LYT-100 (deupirfenidone), a clinical therapeutic candidate that we are pursuing for the potential treatment of a range of conditions involving inflammation and fibrosis and disorders of lymphatic flow, LYT-200, a clinical immuno-oncology fully human monoclonal antibody candidate targeting a foundational immunosuppressive protein, galectin-9, that we are developing for the potential treatment of difficult-to-treat solid tumors, LYT-210, a preclinical immuno-oncology therapeutic candidate targeting immunomodulatory gamma delta-1 T cells that we are developing for a range of cancer indications, LYT-300 (oral allopregnanolone), a clinical therapeutic candidate that we are developing for a range of neurological and neuropsychological conditions, which was generated from our Glyph™ lymphatic targeting platform, and three therapeutic candidates generated from Alivio™, our technology platform that enables targeting of therapeutics locally to the sites of inflammation while minimizing systemic exposure, for the potential treatment of a range of chronic and acute inflammatory disorders: LYT-510 (oral immunosuppressant molecule), in development for the potential treatment of inflammatory bowel disease (IBD) and chronic pouchitis, LYT-500 (oral combination of two therapeutic agents), in development for the potential treatment of mucosal barrier damage in people with IBD, and LYT-503/IMB-150, which is a partnered program being advanced as a potential non-opioid treatment for interstitial cystitis or bladder pain syndrome (IC/BPS). In addition to these programs, we are advancing Orasome™ and other Technology Platforms for the oral administration of therapeutics. Finally, we are pursuing our meningeal lymphatics research program to develop potential treatments for neurodegenerative and neuroinflammatory diseases. In addition to programs originating from these innovative platforms to fuel our pipeline, we also continually identify external clinical-stage programs that are highly differentiated and complementary to the immuno-modulation focus of our Wholly Owned Pipeline.

2 For more information in relation to the PureTech Level Cash and Cash Equivalents and Consolidated Cash and Cash Equivalents measures used in this Annual Report, please see pages 97 and 98 of the Financial Review. At prior comparative periods from 2016 to 2019, balances included cash, cash equivalents and short-term investments. For more information in relation to the PureTech Level Cash Reserves and Consolidated Cash Reserves measures, please also see pages 97 and 98 of the Financial Review.

3 Funding figure includes private equity financings, loans and promissory notes, public offerings or grant awards. Funding figure excludes future milestone considerations received in conjunction with partnerships and collaborations. Funding figure does not include Gelesis' gross proceeds of approximately $105.0 million from its January 2022 post-period SPAC merger.

4 Number represents figure for the relevant fiscal year only and is not cumulative.

5 References in this report to "Wholly Owned Programs" refer to the Company's seven therapeutic candidates (LYT-100, LYT-200, LYT-210, LYT-300, LYT-510, LYT-500 and LYT-503/IMB-150), four lymphatic and inflammation platforms and potential future therapeutic candidates and platforms that the Company may develop or obtain. References to "Wholly Owned Pipeline" refer to LYT-100, LYT-200, LYT-210, LYT-300, LYT-510, LYT-500 and LYT-503/IMB-150. On July 23, 2021, Imbrium Therapeutics exercised its option to license LYT-503/IMB-150 pursuant to which it is responsible for all future development activities and funding for LYT-503/IMB-150.

Clinical trial initiations[4,6]

11

2020: 6
2019: 6

Clinical trial readouts[4,7]

6

2020: 5
2019: 5

Key developments and progress across PureTech's Wholly Owned Programs include:

- In the January 2022 post-period, we were pleased to announce results from a randomized, double-blind crossover study in healthy older adults demonstrating that approximately 50% fewer subjects treated with LYT-100 (deupirfenidone) experienced gastrointestinal (GI)-related adverse events (AE) compared to subjects treated with pirfenidone (17.4% vs. 34.0%). Based on these results, discussions with our Clinical Advisory Board that includes many of the world's leading experts in idiopathic pulmonary fibrosis (IPF) clinical development, additional data generated from our robust LYT-100 clinical program as well as recent regulatory feedback, we intend to advance LYT-100 into late-stage clinical development for the treatment of IPF, beginning with a dose-ranging study evaluating six months of treatment with LYT-100 with topline results expected by the end of 2023.
- In 2021, we progressed two Phase 2 clinical trials of LYT-100 including 1) a global, randomized, double-blind, placebo-controlled Phase 2 trial to evaluate the efficacy, safety and tolerability of LYT-100-COV in adults with Long COVID[8] respiratory complications and related sequelae and 2) a Phase 2a proof-of-concept study of LYT-100-LYMPH in patients with breast cancer-related, upper limb secondary lymphedema. Topline results from the LYT-100-COV trial are expected in the first half of 2022, and topline results from the LYT-100-LYMPH trial are expected in 2022.
- In 2021, we also initiated a three-month, open-label extension of the LYT-100-COV Phase 2 trial in adults with Long COVID respiratory complications and related sequelae who completed the first portion of the trial. The primary endpoint of the extension trial will measure change in distance walked on the six-minute walk test (6MWT), with secondary endpoints to assess the longer-term safety and tolerability of LYT-100-COV up to 182 days of treatment.
- In 2021, we initiated additional clinical studies to further evaluate the pharmacokinetic (PK), dosing and tolerability of LYT-100 in healthy volunteers and healthy older adults to inform the clinical development of LYT-100 across multiple indications. Results from these studies demonstrated that LYT-100 was well-tolerated at 824mg TID dosing with low rates of GI AEs that were comparable to placebo. These results will further inform our dose-ranging study design in treatment-naïve IPF patients.
- In 2021, we continued to build our clinical development team by bringing together seasoned experts focused on tackling diseases with significant unmet medical needs. Julie Krop, M.D., was appointed as Chief Medical Officer. Dr. Krop oversees all clinical development, regulatory, CMC and medical affairs for advancing our Wholly Owned Pipeline. Other additions to our team included Paul Ford, M.D., Ph.D., SVP of Clinical Development who is primarily overseeing the overall LYT-100 development program, including for IPF. We also formed a Clinical Advisory Board for IPF and other progressive fibrosing interstitial lung diseases (PF-ILDs). These physicians and researchers with deep expertise in the clinical development of novel therapies in PF-ILDs include Bill Bradford, M.D., Ph.D., biopharma advisor with broad expertise in drug development; Vincent Cottin, M.D., Professor of Respiratory Medicine at Université Claude Bernard Lyon and Coordinator of the National Coordinating Reference Center for Rare Pulmonary Diseases at Louis Pradel Hospital, Hospices Civils de Lyon, Lyon, France; Kevin Flaherty, M.D., Professor at the University of Michigan specializing in IPF and other ILDs; Toby Maher, M.D., Ph.D., Professor of Clinical Medicine and Director of Interstitial Lung Disease at Keck School of Medicine of the University of Southern California; Paul Noble, M.D., Chair of the Department of Medicine at Cedars-Sinai Medical Center and a noted researcher in lung inflammation and fibrosis; and Marlies Wijsenbeek, M.D., Ph.D., pulmonary physician at the Erasmus Medical Center.
- In the March 2022 post-period, we appointed Sharon Barber-Lui to our board of directors as a non-executive director and as a member of the Audit Committee. She previously led U.S. Oncology Portfolio Strategy, Operations and Business Analytics at Merck & Co. Inc. Ms. Barber-Lui brings extensive experience in finance, operations, portfolio management and commercialization to our board of industry, business and academic leaders.

6 PureTech initiated five clinical trials, Karuna initiated four clinical trials, Vor Bio initiated one clinical trial and Akili initiated one clinical trial in 2021.
7 PureTech (two), Karuna (one), Gelesis (one), and Vedanta (two) reported clinical results from across their pipelines in 2021.
8 Long COVID is a term being used to describe the emerging and persistent complications following the resolution of COVID-19 infection, also known as post-acute COVID-19 syndrome (PACS).

- In August 2021, we presented the results of the Phase 1 multiple ascending dose and food effect study of LYT-100 at the virtual European Respiratory Society (ERS) International Congress. The results from the study were subsequently published in the journal *Clinical Pharmacology in Drug Development* in November 2021.
- In 2021, we progressed the first stage of an adaptive Phase 1/2 clinical trial evaluating LYT-200 (anti-galectin-9 fully human monoclonal antibody) as a single agent for the potential treatment of difficult-to-treat solid tumors. In November 2021, we presented a scientific poster describing the trial at the Society for Immunotherapy of Cancer (SITC) 36th annual meeting. Topline results from the Phase 1 portion of the study are expected in the first half of 2022. Pending these results, we intend to initiate the Phase 2 expansion cohort portion of the trial, which is designed to evaluate LYT-200 both as a single agent and/or in combination with BeiGene's tislelizumab, an anti-PD-1 monoclonal antibody, or chemotherapy. The Phase 2 portion of the study is currently planned to enroll patients with a range of solid tumor types, including pancreatic cancer and other GI solid tumors. Under the terms of the clinical trial and supply agreement we entered into with an affiliate of BeiGene, Ltd. in July 2021, we will maintain control of the LYT-200 program, including global R&D and commercial rights, and BeiGene has agreed to supply tislelizumab for use in combination with LYT-200 for the planned Phase 2 study cohorts.
- In November 2021, the FDA granted orphan drug designation to LYT-200 for the treatment of pancreatic cancer. The FDA grants orphan drug designation to novel drug and biologic products for the treatment, diagnosis or prevention of conditions affecting fewer than 200,000 persons in the U.S. Orphan drug designation qualifies PureTech for incentives under the Orphan Drug Act, including tax credits for some clinical trials and eligibility for seven years of market exclusivity in the U.S. if the drug is approved, in addition to our broad intellectual property coverage which can extend the exclusivity into 2038.
- In April 2021, we presented a scientific poster detailing additional promising preclinical results for LYT-210 (anti-gamma-delta-1 fully human monoclonal antibody) at the 2021 American Association for Cancer Research (AACR) Annual Virtual Meeting. The research demonstrated that LYT-210 is both highly specific and highly potent, rapidly inducing cell death of immunomodulatory gamma delta-1 (γδ1) T cells, while sparing other T cells, such as cytotoxic gamma delta T cells, that play important roles in a healthy immune response.
- In December 2021, we initiated a Phase 1 clinical study of LYT-300 (oral allopregnanolone), the first therapeutic candidate generated from our Glyph platform, for the potential treatment of neurological and neuropsychological conditions. The Phase 1 study of LYT-300 involves multiple parts, including the evaluation of a single ascending dose, multiple ascending doses and the effect of food in healthy volunteers. Safety, tolerability and PK will be assessed. Given the $GABA_A$ receptor modulating activity of allopregnanolone, the study will also explore the impact of LYT-300 on beta-EEG, a marker of $GABA_A$ target engagement, thus potentially providing early insights into the mechanistic effects of LYT-300. Results from the study are expected in the second half of 2022 and will be used to inform the design of possible future studies evaluating LYT-300 in indications that could include depression, anxiety, sleep disorders, fragile X tremor-associated syndrome, essential tremor and epileptic disorders, among others.
- In June 2021, we announced the acquisition of the remaining 22% of outstanding shares in our Founded Entity, Alivio Therapeutics ('Alivio'). Alivio's therapeutic candidates, in development for inflammatory disorders including IBD, have been integrated into our Wholly Owned Pipeline, and the underlying Alivio technology platform has been added to our lymphatic and inflammation platforms. The Alivio technology platform has generated three therapeutic candidates, including LYT-510, an orally-administered therapeutic candidate for the potential treatment of IBD and chronic pouchitis, LYT-500, an oral therapeutic candidate that we are developing for the potential treatment of mucosal barrier damage in people with IBD, and LYT-503/IMB-150 for the potential treatment of IC/BPS (being developed as a partnered program). We expect preclinical proof-of-concept data for LYT-500 in the first half of 2022. We intend to file for regulatory approval to initiate first-in-human studies at year end 2022 and initiate a clinical study evaluating LYT-510 as a single agent for the potential treatment of IBD and chronic pouchitis in early 2023. An IND application for LYT-503/IMB-150 is expected to be filed in 2022.
- In September 2021, preclinical proof-of-concept research supporting the Glyph technology platform, which showed for the first time that restoring normal function of the mesenteric lymphatics may reverse insulin resistance and modify obesity-associated metabolic disease, was published in *Nature Metabolism*. Preclinical proof-of-concept work published in the *Journal of Controlled Release* in February 2021 also supported the platform's ability to directly target the lymphatic system.
- In April 2021, preclinical work supporting our meningeal lymphatics research program was published in *Nature*. The research suggests that restoring lymphatic flow in the brain, either alone or in combination with passive immunotherapies such as antibodies directed at amyloid beta, has the potential to address a range of neurodegenerative diseases, including Alzheimer's and Parkinson's diseases and the associated neuroinflammation. The work also uncovered a link between dysfunctional meningeal lymphatics and damaging microglia activation in Alzheimer's disease, which potentially impairs the efficacy of passive immunotherapies such as amyloid-beta-targeting antibodies. This suggests another route by which restoring healthy drainage patterns could improve clinical outcomes.
- In 2021, we also progressed versatile and programmable oral biotherapeutics approaches, such as our Orasome platform, which is a novel programmable and scalable approach for the oral administration of nucleic acids and other biologics. We established preclinical proof-of-concept supporting the platform's potential to achieve therapeutic levels of proteins in circulation following the oral administration of therapeutic protein expression systems. We expect to generate additional preclinical data, with Orasomes and other technologies, in 2022.

Founded Entities[9]

PureTech's Founded Entities have made significant progress advancing 20 therapeutics and therapeutic candidates, of which two have been cleared for marketing by the FDA and granted marketing authorization in the European Economic Area and 13 are clinical stage. Key developments included the following:

KARUNA THERAPEUTICS

Karuna Therapeutics, Inc. (PureTech ownership: 5.6%; We also are eligible to receive payments under our license agreement, including sublicense payments and royalties on net sales)

- In November 2021, Karuna announced further updates to the EMERGENT program's four ongoing Phase 3 trials, including that topline data from EMERGENT-2, a five-week inpatient trial evaluating the efficacy and safety of KarXT compared to placebo in 246 adults with schizophrenia in the U.S., are expected in mid-2022. EMERGENT-3, a five-week inpatient trial evaluating the efficacy and safety of KarXT compared to placebo in 246 adults with schizophrenia in the U.S. and Ukraine, is underway. EMERGENT-4, a 52-week outpatient, open-label extension trial evaluating the long-term safety and tolerability of KarXT in 350 adults with schizophrenia who completed EMERGENT-2 or EMERGENT-3, and EMERGENT-5, a 52-week outpatient, open-label trial evaluating the long-term safety and tolerability of KarXT in adults with schizophrenia who were not enrolled in EMERGENT-2 or EMERGENT-3, are also underway.
- In 2021, Karuna initiated the Phase 3 ARISE trial evaluating the safety and efficacy of KarXT compared to placebo as an adjunctive treatment in adults with schizophrenia who experience an inadequate response to current standard of care.
- In June 2021, Karuna announced data from its completed Phase 1b trial evaluating the safety and tolerability of KarXT in healthy elderly volunteers, which followed a preliminary analysis of data from the first two cohorts in the trial announced earlier this year. The results suggest that KarXT can be administered to elderly volunteers at doses which achieve xanomeline blood levels similar to those reported in the Phase 2 EMERGENT-1 trial in adults with schizophrenia while maintaining a favorable tolerability profile. Data from the trial also suggest that a lower dose ratio of trospium to xanomeline, compared to the ratios used in Phase 1 trials in healthy adult volunteers and in the Phase 2 EMERGENT-1 trial evaluating KarXT in adults with schizophrenia, was better tolerated by healthy elderly volunteers.
- In November 2021, Karuna announced the evaluation of KarXT for the treatment of dementia-related psychosis (DRP) will initially focus on psychosis in Alzheimer's disease, the most common subtype of DRP. The initial focus on the Alzheimer's disease dementia subtype reflects various strategic development, regulatory and commercial considerations, and Karuna remains interested in exploring KarXT in other dementia subtypes in future development programs. Karuna plans to initiate a Phase 3 program in mid-2022.
- In late 2021, Karuna initiated a Phase 1 trial of an advanced formulation of KarXT as it continued to advance its earlier pipeline of muscarinic receptor targeted programs and novel formulations of KarXT. Karuna is also advancing its artificial intelligence-based target agnostic discovery program for treating psychiatric and neurological conditions.
- In November 2021, Karuna announced its entry into an exclusive license agreement with Zai Lab for the development, manufacturing and commercialization of KarXT in Greater China, including mainland China, Hong Kong, Macau and Taiwan. Under the terms of the agreement, Karuna received a $35.0 million upfront payment and is eligible to receive certain development and regulatory milestone and sales milestone payments, as well as royalties based on annual net sales of KarXT in Greater China.
- In February 2021, Karuna announced that results from the EMERGENT-1 Phase 2 clinical trial evaluating KarXT for the treatment of schizophrenia were published in the *New England Journal of Medicine* (NEJM).
- In March 2021, Karuna completed a follow-on public offering of its common stock, from which it received net proceeds of $270.0 million.
- In 2021, PureTech sold 1,750,000 shares of Karuna common stock for a cash consideration of approximately $218 million in two separate transactions in February and November.

9 While PureTech maintains ownership of equity interests in its Founded Entities, the Company does not, in all cases, maintain control over these entities (by virtue of (i) majority voting control and (ii) the right to elect representation to the entities' board of directors) or direct the management and development efforts for these entities. Consequently, not all such entities are consolidated in the financial statements. Where PureTech maintains control, the entity is referred to as a Controlled Founded Entity in this report and is consolidated in the financial statements. Where PureTech does not maintain control, the entity is referred to as a Non-Controlled Founded Entity in this report and is not consolidated in the financial statements. As of December 31, 2021, Controlled Founded Entities include Follica Incorporated, Vedanta Biosciences, Inc., Sonde Health, Inc. and Entrega, Inc., and Non-Controlled Founded Entities include Gelesis Holdings, Inc., Karuna Therapeutics, Inc., Akili Interactive Labs, Inc., Vor Bio Inc.

AKILI

Akili Interactive Labs, Inc. (PureTech ownership: 22.3%)

- In the January 2022 post-period, Akili entered into a definitive agreement to become publicly traded via a merger with Social Capital Suvretta Holdings Corp. I ("SCS") (Nasdaq: DNAA), a special purpose acquisition company. The transaction is expected to close in mid-2022, after which Akili will be listed on the Nasdaq stock market under the new ticker symbol "AKLI". The transaction implies a post-money equity value of the combined company of up to approximately $1 billion and is expected to deliver up to $412 million in gross cash proceeds to Akili, including the contribution of up to $250 million of cash held in SCS's trust account and $162 million from PIPE investors at $10 per share.
- In May 2021, Akili announced the closing of a $160 million combined equity and debt financing. With the completion of the oversubscribed Series D financing, the funding is expected to accelerate commercialization of EndeavorRx®[10], enable expansion of core technologies to treat acute and chronic cognitive disorders and drive further research and development of potential new digital therapeutics.
- In March 2021, the full data from a multi-site open-label study (the STARS Adjunct study) evaluating the impact of EndeavorRx (AKL-T01) on symptoms and functional impairments in children with attention-deficit/hyperactivity disorder (ADHD) was published in *Nature Digital Medicine*. Statistically significant improvement was demonstrated in all predetermined endpoints of the study, which included parent and clinician ratings of children's ADHD symptoms and related impairments in daily life.
- In the February 2022 post-period, Akili announced the publication of full data in the medical journal *PLOS ONE* from a single arm, unblinded study conducted by Dr. Elysa Marco at Cortica Healthcare and Drs. Joaquin Anguera and Courtney Gallen at the University of California, San Francisco. The study measured electroencephalography (EEG) data alongside behavioral and clinical metrics of attention in children with ADHD using AKL-T01 (EndeavorRx). Data from the study show that EndeavorRx treatment resulted in increased brain activity related to attention function, as measured by EEG, which correlated with improvements in objective behavioral measures of attention.
- In September 2021, Akili announced topline results of a Phase 2 study of SDT-001 (Japanese version of AKL-T01), a digital therapeutic designed to improve measures of attention in children diagnosed with attention-deficit/hyperactivity disorder (ADHD). The study, conducted by Akili partner Shionogi & Co., Ltd., was designed to evaluate the feasibility, safety and efficacy of the digital therapeutic in children with ADHD and to inform the design of a potential pivotal study. Results showed the treatment was well-received by patients and demonstrated improvements in ADHD inattention symptoms consistent with those seen across previous studies of AKL-T01.
- In the March 2022 post-period, Akili announced it had been named to *Fast Company*'s prestigious list of the World's Most Innovative Companies for 2022. This list honors businesses that are making the biggest impacts on their industries and culture as a whole and thriving in today's ever-changing world.
- In July 2021, Akili introduced new gaming features and functionalities to its EndeavorRx treatment. Akili is releasing these new gameplay features as it expands its pre-launch activities to bring EndeavorRx to families and healthcare professionals.
- In April 2021, Akili announced collaborations with Weill Cornell Medicine, New York-Presbyterian Hospital and Vanderbilt University Medical Center to evaluate Akili digital therapeutic AKL-T01 as a treatment for patients with cognitive dysfunction following COVID-19 (also known as "COVID fog"). Under each collaboration, Akili will work with research teams at each institution to conduct two separate randomized, controlled clinical studies evaluating AKL-T01's ability to target and improve cognitive functioning in COVID-19 survivors who have exhibited a deficit in cognition. Akili expects data from the studies in COVID fog in the second half of 2022.
- In August 2021, Akili and Australian digital health company TALi® (ASX:TD1), completed an agreement for Akili to license TALi's technology designed to address early childhood attention impairments. The companies plan to work together to execute clinical trials of the TALi technology in pediatric ADHD in the U.S. and pursue FDA regulatory clearance. Under the terms of the agreement, Akili will lead potential U.S. commercialization and roll-out.
- In the March 2022 post-period, Akili appointed Jon David as Chief Product Officer. A 20-year veteran of the games industry, Mr. David joins Akili to develop and execute the strategic vision of Akili's future product pipeline after serving as Vice President and General Manager at Glu Mobile, acquired in 2021 by Electronic Arts, where he led the development of both new IP and hit franchises including *Covet Fashion* and *Diner Dash Adventures*. Mr. David also guided the success of fan-favorite franchises and the launches of hit titles including *Plants vs. Zombies 2* and *Plants vs. Zombies Garden Warfare*.

10 EndeavorRx® is a digital therapeutic indicated to improve attention function as measured by computer-based testing in children ages 8-12 years old with primarily inattentive or combined-type ADHD, who have a demonstrated attention issue. Patients who engage with EndeavorRx demonstrate improvements in a digitally assessed measure, Test of Variables of Attention (TOVA®) of sustained and selective attention and may not display benefits in typical behavioral symptoms, such as hyperactivity. EndeavorRx should be considered for use as part of a therapeutic program that may include clinician-directed therapy, medication, and/or educational programs, which further address symptoms of the disorder. There were no serious adverse events; 9.3% of subjects experienced side effects, including frustration, headache, dizziness, emotional reaction, nausea or aggression. EndeavorRx is only available to your patients through a prescription, and is not intended as a stand-alone therapeutic or a substitute for your patient's medication.

GELESIS

Gelesis Holdings, Inc. (PureTech ownership: 23.5%; We also are eligible to receive payments under our license agreement, including sublicense payments and royalties on net sales)

- In December 2021, Gelesis announced that Plenity®[11] is now broadly available across the U.S. to adults who meet the prescription criteria.
- In the January 2022 post-period, Gelesis announced the completion of its business combination with Capstar Special Purpose Acquisition Corp. (NYSE: CPSR) ("Capstar"). Gelesis Holdings, Inc. began trading on the New York Stock Exchange under the ticker symbol "GLS" on January 14, 2022.
- In January 2022 post-period, Gelesis launched the "Who Said?" marketing campaign across the U.S., which challenges many long-held cultural and societal assumptions around weight loss. Plenity's multichannel campaign encompasses TV, digital, social and Out of Home (OOH) to grow awareness of Plenity's novel approach to weight management.
- In the March 2022 post-period, Gelesis announced preliminary results from its broad awareness media campaign, noting that within the first three weeks, the company saw a 3-fold increase in web traffic and 3.5-fold increase in the number of individuals seeking a new prescription compared to previous months when supply was limited.
- In November 2021, Gelesis' first commercial-scale manufacturing line was completed and validated, and the company announced that it had received a $30 million fully paid pre-order, in addition to the $10 million pre-order received in January 2021, for its first commercial product for weight management, Plenity, from Ro, a leading U.S. direct-to-patient healthcare company.
- In late 2021, both primary endpoints were achieved in the Gelesis LIGHT-UP study of GS200 in adults with overweight or obesity who also have prediabetes or type 2 diabetes.
- In November 2021, Gelesis announced a publication in *Nature's Scientific Reports* describing the genesis of the underlying technology and engineering process for Gelesis' non-systemic superabsorbent hydrogels. These new materials were designed to replicate compositional and mechanical properties of raw vegetables, and the paper describes their therapeutic approach for weight management as well as possible future solutions for other gut-related conditions.
- In May 2021, Gelesis presented a scientific poster at the American Association of Clinical Endocrinology (AACE) 2021 Annual Virtual Meeting. The post-hoc analysis showed that treatment for weight management with Plenity decreased a marker for liver fibrosis (the NAFLD fibrosis score) compared to placebo.
- In the January 2022 post-period, Gelesis appointed Inogen Co-Founder and former CFO, Ali Bauerlein, to its Board of Directors and Audit Committee. Ms. Bauerlein brings success in scaling to $300M+ revenue in a direct-to-consumer business model and public company execution as Gelesis plans to scale Plenity to meet growing consumer demand.

VOR

Vor Bio Inc. (PureTech ownership: 8.6%)

- In February 2021, Vor Bio announced the pricing of its initial public offering of common stock on the Nasdaq Global Market under the symbol "VOR". The aggregate gross proceeds to Vor Bio from the offering were approximately $203.4 million, before deducting the underwriting discounts and commissions and other offering expenses payable by Vor Bio.
- In the March 2022 post-period, Vor Bio announced VCAR33 is now made up of two programs with different cell sources. The VCAR33 programs are chimeric antigen receptor T (CAR-T) cell therapy candidates designed to target CD33, a clinically-validated target for AML. $VCAR33^{AUTO}$ uses autologous cells from each patient, and is being studied in an ongoing Phase 1/2 clinical trial sponsored by the National Marrow Donor Program (NMDP) in young adult and pediatric patients with relapsed/refractory AML in a bridge-to-transplant study. $VCAR33^{ALLO}$ uses allogeneic healthy donor-derived cells. Vor Bio also announced it plans to collect initial data on VOR33 from the VBP101 clinical trial and initial clinical data from the $VCAR33^{ALLO}$ program prior to IND submission for the Treatment System following ongoing discussions with the FDA and alongside improved scientific understanding of the differences in T-cell sources.
- In September 2021, the FDA granted Fast Track designation to VOR33, Vor Bio's lead engineered hematopoietic stem cell (eHSC) therapeutic candidate for the treatment of acute myeloid leukemia (AML).
- Vor Bio initiated VBP101, a Phase 1/2a clinical trial of VOR33 for AML patients who currently have limited treatment options and expects to report VOR33's initial clinical data in the second half of 2022.
- In November 2021, Vor Bio announced its first multi-targeted treatment system comprising VOR33-CLL1 multiplex-edited eHSC therapy and VCAR33-CLL1 multi-specific CAR-T therapy. Vor Bio continues to make progress on editing multiple antigens with its eHSC platform.
- In June 2021, Vor Bio announced the build-out of an in-house clinical manufacturing facility in Cambridge, Massachusetts in the same premises as Vor Bio's current headquarters, to support flexible manufacturing for the company's eHSC and CAR-T product candidate pipeline for patients with blood cancers. Vor Bio anticipates that the facility will be operational in 2022.
- In July 2021, Vor Bio announced the formation of a collaboration with Janssen Biotech, Inc. (Janssen), one of the Janssen Pharmaceutical Companies of Johnson & Johnson.

11 Important Safety Information about Plenity®: Patients who are pregnant or are allergic to cellulose, citric acid, sodium stearyl fumarate, gelatin, or titanium dioxide should not take Plenity. To avoid impact on the absorption of medications: For all medications that should be taken with food, take them after starting a meal. For all medications that should be taken without food (on an empty stomach), continue taking on an empty stomach or as recommended by your physician. The overall incidence of side effects with Plenity was no different than placebo. The most common side effects were diarrhea, distended abdomen, infrequent bowel movements, and flatulence. Contact a doctor right away if problems occur. If you have a severe allergic reaction, severe stomach pain, or severe diarrhea, stop using Plenity until you can speak to your doctor. Rx Only. For the safe and proper use of Plenity or more information, talk to a healthcare professional, read the Patient Instructions for Use, or call 1-844-PLENITY.

The agreement was facilitated by Johnson & Johnson Innovation. Under the terms of the collaboration, Vor Bio will investigate the combination of these two technologies into a treatment solution, pairing Vor Bio's "invisible" eHSC transplant platform with one of Janssen's bi-specific antibodies in development for AML. The collaboration agreement provides that each company retains all rights and ownership to their respective programs and platforms.

- In June 2021, Vor Bio entered into a multi-year strategic collaboration and license agreement with Abound Bio to research both single- and multi-targeted CAR-T treatments to be used in combination with Vor Bio's eHSC platform, with the goal of generating novel treatment systems for patients fighting AML and other devastating forms of blood cancer.
- In January 2021, Vor Bio announced that the FDA had accepted the company's IND application for VOR33. In May 2021, Vor Bio announced that it received the Canadian clinical trial application clearance for VOR33 from Health Canada.
- In June 2021, Vor Bio announced the appointment of Matthew R. Patterson as Chairman of its Board of Directors. Mr. Patterson brings nearly 30 years of senior leadership experience in the research, development and commercialization of innovative therapeutics, most recently at Audentes Therapeutics, Inc., which he co-founded and led as the company's Chief Executive Officer from its inception in 2012 through its acquisition by Astellas Pharma Inc. in January 2020.

VEDANTA BIOSCIENCES

Vedanta Biosciences, Inc. (PureTech ownership: 41.4%)

- In October 2021, Vedanta announced that its Phase 2 clinical trial of VE303, an orally administered investigational live biotherapeutic product (LBP) in development for the prevention of recurrent *C. difficile* infection (CDI) in high-risk patients, met its primary endpoint of preventing disease recurrence through Week 8. VE303 achieved a 31.7% absolute risk reduction in rate of recurrence when compared with placebo, representing a greater than 80% reduction in the odds of a recurrence. This is believed to be the most advanced clinical trial of an investigational drug based on a rationally defined bacterial consortium, a microbiome-based therapeutic approach that delivers orally administered candidates of precisely known composition that can be manufactured with pharmaceutical-grade consistency. Based on the Phase 2 data, the Biomedical Advanced Research and Development Authority (BARDA) exercised its first contract option for additional funding of $23.8 million, pursuant to its existing 2020 contract with Vedanta, to support a planned Phase 3 clinical trial of VE303.
- In January 2021, Vedanta announced a $25 million investment from Pfizer, as part of the Pfizer Breakthrough Growth Initiative. Vedanta will retain control of all of its programs and has granted Pfizer a right of first negotiation on VE202, Vedanta's 16-strain defined bacterial consortium candidate. As part of the investment, Michael Vincent, M.D., Ph.D., Senior Vice President and Chief Scientific Officer, Inflammation & Immunology Research Unit at Pfizer, joined Vedanta's Scientific Advisory Board.
- In late 2021, Vedanta also completed the build-out of its Phase 3 and commercial launch CGMP manufacturing facility for supply of VE303.
- In June 2021, Vedanta presented additional results from a Phase 1 study in healthy volunteers of VE202, Vedanta's 16-strain defined bacterial consortium candidate for IBD, at the International Human Microbiome Consortium Congress 2021 (IHMC). The data summarized the long-term safety and colonization dynamics of the 16-strain version of VE202 in 31 healthy volunteers. Vedanta plans to initiate a Phase 2 clinical trial of VE202 in mild to moderate ulcerative colitis patients.
- In 2021, Vedanta's ongoing Phase 1/2 clinical trial of VE416 for food allergy continued to progress.
- In July 2021, Vedanta announced results from the Phase 1 study evaluating the safety and initial clinical activity of VE800, and immuno-oncology therapeutic candidate, in combination with Bristol Myers Squibb's Opdivo® (nivolumab) in 54 patients across select types of advanced or metastatic cancers. VE800 demonstrated an acceptable safety and tolerability profile, though the observed response rates did not meet the prespecified criteria to advance into the next stage of the study. Vedanta is analyzing blood, stool and tumor samples from patients in whom response or disease control was observed in order to profile patient subtypes that might benefit from microbiome manipulation. Vedanta plans to present the results at a future medical conference and will continue work to identify cancer settings and patient populations that might benefit from microbiome manipulation with its defined bacterial consortia.
- In July 2021, Vedanta closed a $68 million financing, which included the $25 million investment from Pfizer as part of the Pfizer Breakthrough Growth Initiative announced in January 2021. Vedanta plans to use the proceeds to advance its pipeline of defined bacterial consortia, including progressing VE303 into a Phase 3 clinical trial in patients at high risk for recurrent CDI, initiating a Phase 2 clinical trial of VE202 in mild to moderate ulcerative colitis and continuing to advance programs in additional indications.
- In February 2021, Vedanta appointed Mark Mullikin as Chief Financial Officer. Mr. Mullikin brings 25 years of experience raising and deploying capital for life sciences companies, and most recently held leadership roles in finance and investor relations at publicly-traded companies such as Editas Medicine and Novartis.
- In October 2021, Vedanta announced the appointment of Simona Levi, Ph.D., J.D., as Chief Legal Officer and Corporate Secretary. Dr. Levi brings over 25 years of U.S. and international legal experience with private and public companies across the life sciences industry focusing on complex transactions, intellectual property law and litigation as well as corporate governance.

follica

Follica, Incorporated (PureTech ownership: 76.0%. We also are eligible to receive payments under our license agreement, including sublicense payments and royalties on net sales)

- In January 2021, Follica announced the appointment of two leaders in aesthetic medicine and dermatology to its Board of Directors. Tom Wiggans, former Chief Executive Officer of Dermira, joined as Executive Chairman with over 30 years of experience leading biopharmaceutical companies from the start-up stage to global commercialization, and Michael Davin, former Chief Executive Officer of Cynosure, joined as an Independent Director with over 30 years of experience in the medical device industry.
- Preparations are underway for the registration clinical program in male androgenetic alopecia and initiation is anticipated in 2022.

SONDE

Sonde Health, Inc. (PureTech ownership: 44.6%)

- In October 2021, Sonde launched Sonde Mental Fitness, a voice-enabled mental health detection and monitoring technology that uses a brief voice sample to evaluate mental well-being. Sonde Mental Fitness is currently available through its API platform for integration into third-party apps. It's also available as a standalone app for iOS and Android, mobile devices to serve as a proof-of-concept for health systems, employers and wellness services interested in testing out the API's capabilities.
- In the January 2022 post-period, Sonde announced the signing of a multi-year strategic partnership with GN Group to research and develop commercial vocal biomarkers for mild cognitive impairment. The research will serve as the backbone for new voice-based tools to help at-risk individuals gain timely and accurate health insights using GN Group's device technologies and, ultimately, to enable early detection and management of life-threatening diseases for the millions of people living with hearing loss.
- In July 2021, Sonde announced a strategic collaboration with leading chipmaker Qualcomm Technologies, Inc. (Qualcomm) to embed Sonde's vocal biomarker technology into its flagship and high-tier Qualcomm® Snapdragon™ 888 and 778G 5G Mobile Platforms to help bring native, machine learning-driven vocal biomarker capabilities to mobile and IoT devices globally. The optimization has the potential to unlock several native health screening and monitoring applications on up to the hundreds of millions of mobile devices that use these Snapdragon mobile platforms.

entrega

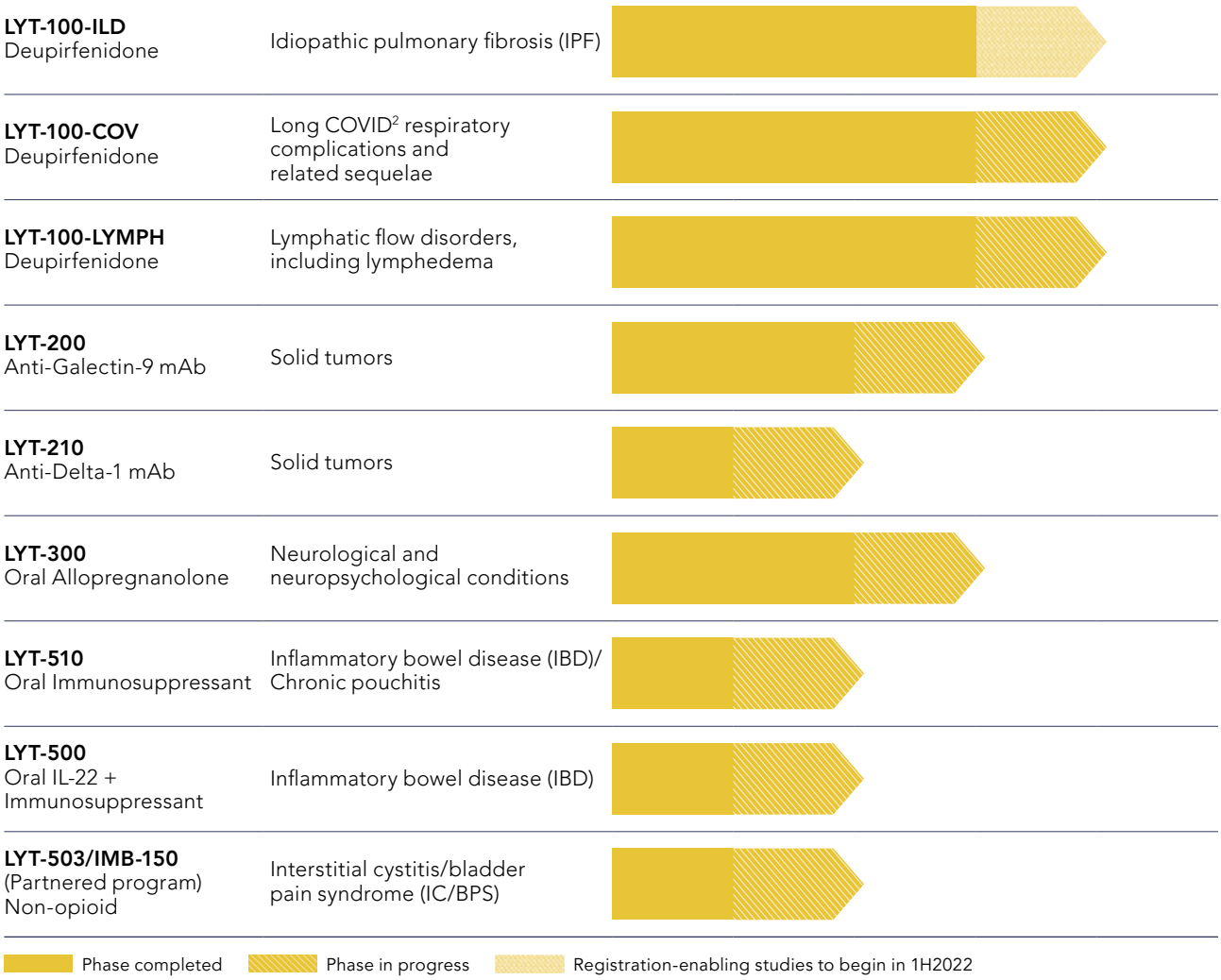
Entrega, Inc. (PureTech ownership: 74.3%)

- Entrega continued to advance its platform for the oral administration of biologics, vaccines and other drugs that are otherwise not efficiently absorbed when taken orally. As part of its collaboration with Eli Lilly, Entrega has continued to investigate the application of its peptide administration technology to certain Eli Lilly therapeutic candidates. The partnership has been extended into 2022.
- Entrega has also continued advancement of its ENT-100 platform for the oral administration of biologics, vaccines and other drugs that are otherwise not efficiently absorbed when taken orally.

Components of Value

Wholly Owned Pipeline

Our programs[1]	Indication
LYT-100-ILD Deupirfenidone	Idiopathic pulmonary fibrosis (IPF)
LYT-100-COV Deupirfenidone	Long COVID[2] respiratory complications and related sequelae
LYT-100-LYMPH Deupirfenidone	Lymphatic flow disorders, including lymphedema
LYT-200 Anti-Galectin-9 mAb	Solid tumors
LYT-210 Anti-Delta-1 mAb	Solid tumors
LYT-300 Oral Allopregnanolone	Neurological and neuropsychological conditions
LYT-510 Oral Immunosuppressant	Inflammatory bowel disease (IBD)/ Chronic pouchitis
LYT-500 Oral IL-22 + Immunosuppressant	Inflammatory bowel disease (IBD)
LYT-503/IMB-150 (Partnered program) Non-opioid	Interstitial cystitis/bladder pain syndrome (IC/BPS)



Lymphatic and Inflammation Platforms

- Glyph™ Technology Platform (Lymphatic Targeting)
- Orasome™ and Other Technology Platforms (Oral Biotherapeutics)
- Alivio™ Technology Platform (Inflammation Targeting)
- Meningeal Lymphatics Research Program

Cash at PureTech Level

$418.9m PureTech Level Cash and Cash Equivalents as of December 31, 2021[3]

1 The FDA and corresponding regulatory authorities will ultimately review our clinical results and determine whether our wholly-owned therapeutic candidates are safe and effective. No regulatory agency has made any such determination that our wholly-owned therapeutic candidates are safe or effective for use by the general public for any indication.

2 Long COVID is a term being used to describe the emerging and persistent complications following the resolution of COVID-19 infection, also known as post-acute COVID-19 syndrome (PACS).

3 For more information in relation to the PureTech Level Cash and Cash Equivalents and Consolidated Cash and Cash Equivalents measures used in this Annual Report, please see pages 97 and 98 of the Financial Review.

Founded Entities[4]

Advancing transformative medicines for people living with psychiatric and neurological conditions

Interest[5]
5.6% Equity plus Royalties, Milestone Payments & Sublicense Revenues

Stage of Development
Phase 3

Nasdaq
KRTX

Pioneering the development of cognitive treatments through game-changing technologies

Interest[5]
22.3% Equity

Stage of Development
Commercial

Advancing a novel category of treatments for weight management and gut related chronic diseases

Interest[5]
23.5% Equity plus Royalties

Stage of Development
Commercial

NYSE
GLS

Engineering hematopoietic stem cell therapies combined with targeted therapies

Interest[5]
8.6% Equity

Stage of Development
Phase 1/2a

Nasdaq
VOR

Pioneering a new category of oral therapies based on defined bacterial consortia

Interest[5]
41.4% Equity

Stage of Development
Phase 3 Ready

Building a regenerative biology platform for androgenetic alopecia, epithelial aging and other medical indications

Interest[5]
76.0% Equity plus Royalties

Stage of Development
Phase 3 Ready

Developing a voice-based technology platform to detect changes of health conditions

Interest[5]
44.6% Equity

Stage of Development
Commercial Release

Engineering hydrogels to enable the oral administration of biologics

Interest[5]
74.3% Equity

Stage of Development
Preclinical

4 This figure represents the stage of development for each Founded Entity's most advanced therapeutic candidate. For additional information, please see footnote no. 9 on page 5.

5 Relevant ownership interests for Founded Entities contained in this strategic report (pages 2-72) were calculated on a partially diluted basis (as opposed to a voting basis) as of December 31, 2021, including outstanding shares, options and warrants, but excluding unallocated shares authorized to be issued pursuant to equity incentive plans. Vor Bio, Karuna and Gelesis ownerships were calculated on a beneficial ownership basis in accordance with SEC rules as of March 4, 2022 and February 15, 2022 and March 31, 2022, respectively.

Letter from the Chair

"In my experience, very few companies come anywhere close to PureTech's realization of a truly innovative business and development model that has established a foundation for long-term growth."

Christopher Viehbacher,
Chair of the Board of Directors

The past year has been a highly dynamic one for the biotech industry. With vaccines and therapies against COVID-19 taking center stage in the public consciousness, investment in life sciences companies soared and then public companies faced headwinds. The pace of incredible innovation across a wide range of therapeutic modalities and diseases accelerated. The fundamental opportunity we have to bring transformative medicines to people in need has never been larger or more achievable. Research tools grow more powerful at an accelerating pace, and we are steadily building the evidence base for many innovative platforms with the potential to fill pipelines of breakthrough medicines in the years to come.

PureTech represents the most compelling elements of the biotherapeutics industry in a single company. We leverage world-leading expertise in immunology and the brain, immune and gastrointestinal systems to address serious debilitating diseases. We prioritize harnessing validated biology to advance differentiated therapeutic candidates with well-managed risk profiles and robust development rationales from day one. The result is a unique pharmaceutical pioneer with a strong track record of innovation and clinical success, an exciting, diversified pipeline of innovative therapeutic candidates and programs, a strong balance sheet and a clear vision for bringing breakthrough new medicines to the patients.

We are moving steadily towards our vision of a fully integrated biotherapeutics company, creating value organically from internally-driven growth while also sourcing programs that complement our strategy and expertise to build a truly differentiated portfolio of high-value new medicines. In my experience, very few companies come anywhere close to PureTech's realization of a truly innovative business and development model that has delivered such a sustainable foundation for long-term growth.

Across our Wholly Owned Pipeline, all our work is united by a mission to deliver highly differentiated medicines for devastating diseases where there are currently limited or no options available for patients. That internal pipeline now includes seven therapeutic candidates. We advanced three of these through the clinic in 2021, most notably in two Phase 2 trials of LYT-100, a Phase 1/2 trial of LYT-200 and a Phase 1 study of LYT-300.

As a highly versatile therapeutic candidate built on substantial validated biology and clinical data, PureTech's lead therapeutic candidate, LYT-100 (deupirfenidone), is rapidly building a compelling expanded clinical profile to address a range of serious fibrotic and inflammatory diseases. Study data announced in late 2021 and the early 2022 post-period have helped paint a picture of a therapeutic with substantially enhanced tolerability relative to pirfenidone, a drug already approved for IPF, a chronic orphan condition that causes progressive scarring of the lungs and has a median survival of 3-5 years.

This de-risked strategy of leveraging validated biology is employed across several of our Wholly Owned Pipeline candidates. It is enhanced by our novel research platform technologies, each of which can be applied to known therapeutic entities, with clinical validation, to generate novel candidates that not only help grow our Wholly Owned Pipeline organically but have the potential to change the treatment paradigm for a range of serious diseases and generate significant value for the patients and our shareholders.

To complement our innovative R&D engine, our Founded Entities are also maturing well, with three of them now publicly traded and a fourth one soon expected to go public, and they continue to generate value for PureTech through their ongoing, independent activity. In 2021, for example, we monetized a portion of our equity in one of our Founded Entities, Karuna Therapeutics, resulting in approximately $218 million being added to PureTech's balance sheet and bringing the total to approximately $565 million generated to date while still maintaining a significant equity stake as one of the largest shareholders and the right to receive royalties and sublicense revenues from the KarXT programs. Our Founded Entities are a source of value to us through potential M&A transactions, equity stakes, royalties and milestone payments as they continue to deliver on their promise. Monetization of our stakes in the Founded Entities has provided us with important resources to advance our Wholly Owned Pipeline.

Collectively, our eight Founded Entities are now advancing 20 therapeutics and therapeutic candidates, of which two have been cleared for marketing by the FDA and granted marketing authorization in the European Economic Area, and 13 are clinical stage.

The Founded Entities continued to mature over the year, with Akili and Gelesis making major strides towards full commercial launches for their groundbreaking products as well as entering the public equity markets. Vor Bio also entered the clinic and completed its initial public offering on Nasdaq.

In the January 2022 post-period, Gelesis became public, raising capital to fuel its commercialization strategy for Plenity®[1] as a truly novel approach for overweight and obesity. Akili also announced its entry into a definitive agreement to become publicly traded via a merger with Social Capital Suvretta. The transaction is expected to close in mid-2022, after which Akili will be listed on the Nasdaq stock market under the new ticker symbol "AKLI".

Diversifying the ways we can create value for shareholders adds stability to our anticipated growth trajectory and – as we have seen – feeds value back into the core enterprise centered on the Wholly Owned Programs. Those programs have substantial potential opportunities in major markets, while the risk profile of the portfolio is offset by our equity holdings, royalties and other payments from our Founded Entities. The resulting balance of opportunity and risk is rare in the biotherapeutics industry, and we are justifiably proud of the model.

Overall, PureTech delivered substantial growth across the Founded Entities and Wholly Owned Pipeline in 2021. Sustaining this momentum over such an extensive range of projects does not happen without a significant unified effort, and I congratulate the hard work and dedication of the PureTech team and its broader network. It is deeply rewarding to work with such a seasoned Board of Directors and management team who translate the Board's guidance into operational excellence and strong partnerships. The grounding focus of our shared passion for helping people with devastating diseases is palpable in our work, and I am convinced it is integral to PureTech's culture and success.

Thank you to all of our shareholders for continuing to support our work for patients. After another year of PureTech evolving into an exemplar for a truly innovative pharmaceutical enterprise, I am humbled by the opportunity to be part of the team's journey and I look forward to continued success in 2022.

Christopher Viehbacher
Chair

April 25, 2022

PureTech's R&D Engine Has Delivered Results[2]

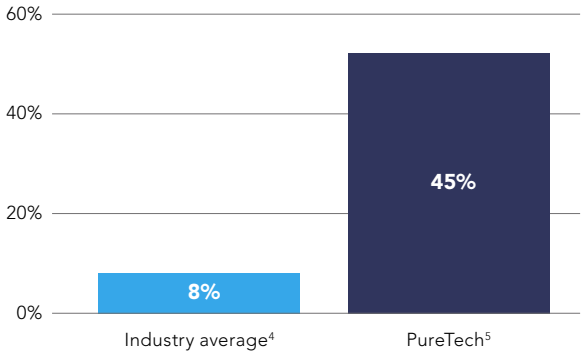
27 new therapeutics and therapeutic candidates

16 clinical stage candidates

2 taken from inception to FDA and EU regulatory clearances

Track Record of Clinical Success[3]

Probability of Transition Success from Ph1 to Regulatory Filing



1 Please see footnote 11 on page 7 for Important Safety Information about Plenity®.

2 PureTech has established the underlying programs and platforms that have resulted in therapeutics and therapeutic candidates that are being advanced within our Wholly Owned Programs or by our Founded Entities. The numbers on this graphic reflects status of those therapeutics and therapeutic candidates as of the date of PureTech's most recently filed Annual Report on Form 20-F.

3 The cumulative percentages are calculated by multiplying the individual phase percentages listed in the following footnotes 4 & 5.

4 Industry average data measures the probability of clinical trial success of therapeutics by calculating the number of programs progressing to the next phase vs. the number progressing and suspended (Phase 1=52%, Phase 2=29%, Phase 3=58%). BIO, PharmaIntelligence, QLS (2021) Clinical Development Success Rates 2011 – 2020. This study did not include therapeutics regulated as devices.

5 The aggregate percentages include all therapeutic candidates advanced through at least Phase 1 by PureTech or its Founded Entities from 2009 onward, using the aforementioned calculation method based on the following individual phase percentages, Phase 1 (n = 6/8; 75%), Phase 2 (n = 10/11; 91%), Phase 3 (n = 2/3; 67%); Phase 2 and Phase 3 percentages include some therapeutic candidates where Phase 1 trials were not conducted by PureTech or its Founded Entities (i) due to the requirements of the medical device regulatory pathway or (ii) because a prior Phase 1 trial was conducted by a third party.

GIVING LIFE TO SCIENCE®

"PureTech is in an enviable position as we build on the momentum of our accomplishments in 2021. Our balance sheet, Founded Entities equity and royalty stakes, and Wholly Owned Programs put us in a stronger position than ever to build value in the current environment and deliver on our mission of bringing breakthrough medicines to patients."

Daphne Zohar,
Founder and Chief Executive Officer

Towards our goal of building value and delivering on our mission of bringing breakthrough medicines to patients, we continue to deliver on the growing value from the hub-and-spoke R&D model that PureTech pioneered for therapeutic development. For years, we developed in-house expertise and a global network of world-class advisors that informed the creation of our Founded Entities (the spokes). The success of several of our Founded Entities as they became independent and are advancing innovative new medicines validated our R&D model and established a strong track record which enables self-sustaining growth, as evidenced by their raising $1.9 billion in aggregate over the last few years. In addition, these Founded Entities are a source of capital to PureTech. To date, we have been able to generate over $560 million in non-dilutive cash while still maintaining strong equity positions. We anticipate further value to us from these entities through events such as M&A transactions or public listings with subsequent value accretion in addition to royalty and milestone payments from commercialized products such as KarXT or Plenity and product candidates in development. We are also structured to potentially receive sublicense revenues from pharma partnerships entered into with certain Founded Entities.

As our balance sheet and track record strengthened, we decided to maintain a group of Wholly Owned Programs to capture more of the value from our core capabilities of identifying and inventing novel medicines and taking them through proof-of-concept. The Wholly Owned Programs and our core areas of expertise around brain, immune and gastrointestinal systems, with a particular focus on immunological disorders, are the hub of our R&D model. In addition, we have consistently demonstrated our ability to harness validated biology and add important innovative steps that enable new medicines to advance. We have been building a differentiated, integrated biopharmaceutical company that develops its own wholly-owned therapeutics as well as benefits from the successes of the now-independent Founded Entities. This gives PureTech a diverse foundation for sustainable growth with a well-managed risk profile.

PureTech's history of building on validated biology has been woven into our strategic framework from our early days. For example, our Founded Entity Karuna's core technology improved upon a clinical compound by addressing tolerability issues and opening up new possibilities in an area of major need where therapeutic innovation has languished – schizophrenia and other serious psychiatric and neurological conditions. This is very similar to our approach to our Wholly Owned Program, LYT-100, in the way of its de-risked clinical profile with a new chemical entity. LYT-100 maintains the pharmacology of pirfenidone with a differentiated PK profile, enabling an improved tolerability profile. We were excited when LYT-100 demonstrated a comparable total exposure to pirfenidone based on PK modeling from prior studies, while improving on the GI-related AEs, as announced in the January 2022 post-period.

Each of our programs is highly innovative and has the potential to change the treatment paradigm for a number of serious diseases. In the same vein as Karuna and LYT-100, LYT-300 from our Glyph™ platform, LYT-510 and LYT-500 from our Alivio™ platform, and Orasome™ programs are reasonably de-risked given they are based on validated biology and pharmacology. We believe that focusing on validated biology therefore offers us an important strategic advantage and confidence as we invest in these programs. I am beyond excited about the progress of our Wholly Owned Programs, especially those that are now in human studies. Our other public Founded Entities, Gelesis and Vor Bio, also harnessed validated biology to create new opportunities for millions of patients as a result of our foundational input.

We are building our Wholly Owned Pipeline based on candidates that emerge from three potentially disruptive technology platforms as well as from thematic sourcing of programs externally.

Our proprietary technology platforms in lymphatics and inflammation are powerful tools for further enabling this strategy. Across our Alivio, Glyph and Orasome and other oral delivery technologies, we have a versatile toolkit for rapidly articulating entirely new target product profiles based on validated biology and pharmacology. An example is LYT-300, an oral allopregnanolone candidate emerging from the Glyph platform. Allopregnanolone is a natural neurosteroid that is approved to treat postpartum depression but is generally poorly orally bioavailable and has to be administered as a 60-hour intravenous infusion. Although efficacious, the intravenous formulation has limited its application. Applying our Glyph technology, we have developed an oral form of natural allopregnanolone (LYT-300) that we are currently evaluating in a first-in-human clinical study. Similarly, we have several molecules with clinically validated biology and pharmacology that we are evaluating

Milestones achieved in 2021

$418.9m PureTech Level Cash and Cash Equivalents as of December 31, 2021[1]

Proven track record of value creation, credibility and transparency

January

Vor Bio announced FDA clearance of IND application for VOR33

February

PureTech generated approximately **$118M** from Founded Entity equity sale[2]

Vor Bio completed **$203.4M** IPO

Karuna's Phase 2 EMERGENT-1 trial of KarXT in schizophrenia published in *NEJM*

PureTech's Glyph preclinical POC study published in *Journal of Controlled Release*

March

Akili's EndeavorRx® clinical study in pediatric ADHD published in *Nature Digital Medicine*

Karuna closed **$270.0M** follow-on public offering

April

Akili announced collaboration with Weill Cornell & Vanderbilt to evaluate AKL-T01 for COVID fog

PureTech's meningeal lymphatics research program published in *Nature*

May

Akili announced the closing of **$160M** Series D

PureTech formed Clinical Advisory Board for IPF and other PF-ILDs

June

PureTech acquired remaining interest in Founded Entity, Alivio Therapeutics

Karuna completed Phase 1b trial of KarXT in healthy volunteers

Vedanta announced presentation of new data from Phase 1 study of VE202 for treatment of IBD

July

Vedanta announced the closing of **$68M** Series D

Gelesis announced SPAC merger with Capstar Special Purpose Acquisition Corp.

Vor Bio announced its collaboration with Janssen Biotech to develop eHSC with a bi-specific antibody therapy for AML

Sonde announced collaboration with Qualcomm Technologies for vocal biomarker technology

PureTech announced clinical trial and supply agreement with BeiGene to evaluate LYT-200 and tislelizumab in solid tumors

August

PureTech appointed Dr. Julie Krop as Chief Medical Officer

Akili announced strategic licensing agreement with TALi

September

Akili announced completion of Shionogi Phase 2 study of SDT-001 in Japan

PureTech's Glyph technology platform published in *Nature Metabolism*

Vor Bio announced FDA granted fast track designation for VOR33

October

Sonde launched Sonde Mental Fitness

Vedanta announced topline Phase 2 data for VE303 and exercise of **$23.8M** option by BARDA

November

Gelesis received **$30M** Plenity® order from Ro

PureTech's LYT-100 Phase 1 results published in the journal *Clinical Pharmacology in Drug Development*

PureTech received orphan drug designation for LYT-200

PureTech generated approximately **$100M** from Founded Entity equity sale[3]

Karuna announced collaboration with Zai Lab for KarXT development, manufacturing, and commercialization of KarXT in Greater China

Gelesis' foundational biomimetic platform published in *Scientific Reports*

December

Gelesis' Plenity® became broadly available in the US

PureTech announced Phase 1 initiation of LYT-300

1 For more information in relation to the PureTech Level Cash and Cash Equivalents and Consolidated Cash and Cash Equivalents measures used in this Annual Report, please see pages 97 and 98 of the Financial Review.
2 Approximately $118 million in proceeds from the February 10, 2021 sale of 1 million Karuna common shares.
3 Approximately $100 million in proceeds from the November 9, 2021 sale of 750,000 Karuna common shares.

utilizing our Glyph, Alivio and Orasome and other oral delivery technologies to breathe new life into these molecules with a highly differentiated profile. We plan to advance one or more of these into clinical development under the Wholly Owned Pipeline.

In addition to the innovation engine of our platforms, we continually identify and seek access to external clinical-stage programs that are highly differentiated and complementary to the immune modulation focus of our Wholly Owned Pipeline.

Looking ahead, we believe our strategy and in-house capabilities strongly position us to build on the value through advancing innovative, differentiated medicines for patients.

The core of our business is advancing innovative medicines, and we believe 2022 will deliver significant growth on that front, with our internal pipeline expecting multiple clinical milestones, new registration-enabling studies, new programs and deepened platform validation.

In addition to research and development excellence, we are executing on a broader strategy to build shareholder value. This includes continuing to strengthen our balance sheet, implementing steps to address the disconnect we believe exists between our valuation and true value and supporting our Founded Entities in their growth and creation. We have also been considering various approaches to drive additional value for our shareholders, including through the implementation of a capital deployment strategy that balances investment in the continued growth of our business with potential returns of capital to shareholders.

Portfolio review

Across the key areas of pipeline development and clinical execution, PureTech continued to deliver. Highlights from the past year include:

Wholly Owned Pipeline

In 2021, our team was proud to welcome Dr. Julie Krop as Chief Medical Officer, who brings deep expertise in regulatory affairs, CMC and clinical development (both as a leader and as a board-certified physician) to oversee the significantly expanded Wholly Owned Pipeline.

- **LYT-100:** In the January 2022 post-period, we were excited to share a successful readout from a Phase 1 trial enrolling a healthy older adult population which demonstrated that 50% fewer subjects experienced GI-related AEs compared to those treated with the FDA-approved drug pirfenidone for IPF. We intend to advance a late-stage clinical program in IPF that will leverage a streamlined 505(b)(2) development path, with topline results from the dose-ranging study expected by the end of 2023. LYT-100 is a selectively deuterated form of pirfenidone that maintains the pharmacology of pirfenidone but has a highly differentiated PK profile that has translated into favorable tolerability, as demonstrated by data from multiple human clinical studies. We have assembled a stellar clinical advisory board of advisors for IPF and related lung disorders to help us advance LYT-100 into registration-enabling studies, and have appointed pulmonary drug development veteran, Paul Ford, M.D., Ph.D., as SVP of Clinical Development to provide additional internal expertise. LYT-100 is also being evaluated in a Phase 2 trial in Long COVID with results expected in the first half of 2022, and a Phase 2a trial in lymphedema with topline results expected in 2022. We are evaluating a range of additional fibrotic conditions for LYT-100, such as radiation induced fibrosis, myocardial fibrosis and other organ system fibrosis.
- **LYT-200/210:** LYT-200 is currently being evaluated as a single agent in the first stage of an adaptive Phase 1/2 trial and we expect to report topline results in the first half of 2022 from this study. Complementing this activity, we entered into a clinical trial and supply agreement with BeiGene to evaluate LYT-200 with BeiGene's tislelizumab, an anti-PD-1 immune checkpoint inhibitor, in patients with difficult-to-treat solid tumors. On the regulatory front, the FDA granted LYT-200 orphan drug designation for pancreatic cancer, which qualifies PureTech for incentives under the Orphan Drug Act, including tax credits for some clinical trials and eligibility for seven years of market exclusivity in the U.S. if the drug is approved. We believe the targeting of a foundational immunosuppressive protein, galectin-9, gives LYT-200 the potential to treat a range of cancers. This year we also presented new research at the American Association for Cancer Research (AACR) Annual Meeting demonstrating that our other fully human monoclonal antibody candidate for cancer, LYT-210, which is both highly specific and highly potent, rapidly inducing cell death of immunomodulatory gamma delta-1 T cells while sparing other T cells that play important roles in a healthy immune response.
- **LYT-300:** We initiated a first-in-human clinical trial of LYT-300, oral allopregnanolone, to evaluate its safety, tolerability and PK profile, as well as its impact on beta-EEG, a marker of $GABA_A$ target engagement, potentially providing early insights into its mechanism. We also presented preclinical proof-of-concept data at the American College of Neuropsychopharmacology (ACNP) Annual Meeting showing that systemic exposure of natural allopregnanolone was achieved after oral administration of LYT-300 in multiple preclinical models. Results from the Phase 1 trial are expected in the second half of 2022 and will be used to inform the design of possible future studies evaluating LYT-300 in indications that could include depression, anxiety, sleep disorders, fragile X tremor-associated syndrome, essential tremor and epileptic disorders, among others.

- On top of the progress of LYT-300 (developed using the Glyph platform), preclinical proof-of-concept work was published in *Nature Metabolism* and the *Journal of Controlled Release* supporting the Glyph technology platform's ability to employ the body's natural lipid absorption and transport process to send oral drugs into the lymphatic system.
- **LYT-510:** LYT-510 is an oral inflammation-targeting formulation of tacrolimus, a potent immunosuppressant drug, in development to treat IBD and chronic pouchitis. In multiple preclinical IBD models, LYT-510 showed significant improvements in several efficacy endpoints compared to untreated controls. Furthermore, the inflammation-targeting properties were shown to result in very low systemic blood levels compared to the current immunosuppressant formulations, which minimizes the potential for systemic side effects. We intend to file for regulatory approval to initiate first-in-human studies at year end 2022 and initiate a clinical study evaluating LYT-510 as a single agent for the potential treatment of IBD and chronic pouchitis in early 2023.
- **LYT-500:** We identified this candidate as a potential therapy for IBD and progressed preclinical evaluation. LYT-500 uses the Alivio platform to combine two active agents (IL-22 and an immunosuppressant drug) into a single therapeutic candidate for IBD that is designed to enhance the treatment of inflamed tissues while having the potential to minimally impact the rest of the body. Proof-of-concept data are expected in the first half of 2022. In addition to the progress of LYT-510 and LYT-500 (developed using the Alivio platform), we are evaluating other potential therapeutic candidates leveraging Alivio to selectively restore immune homeostasis at inflamed sites in the body, while minimalizing impact on the rest of the immune system.
- **LYT-503/IMB-150:** This non-opioid pain candidate being developed as a partnered program for the potential treatment of IC/BPS is expected to be filed for an IND application in 2022.
- **Orasome platform and other technologies for oral administration of biologics:** We have established preclinical proof-of-concept supporting the platform's potential to achieve therapeutic levels of proteins in circulation following oral administration of therapeutic protein expression systems. We intend to generate additional preclinical data in 2022 exploring the potential of Orasomes and other technologies, for a wide array of novel therapeutic protein-based applications.
- **Meningeal lymphatics research program:** We published preclinical research in *Nature* supporting the hypothesis that restoring lymphatic flow in the brain has the potential to address a range of neurodegenerative diseases, such as Alzheimer's and Parkinson's diseases and associated neuroinflammation.

Founded Entities

- **Karuna Therapeutics (Nasdaq: KRTX):** Announced that all four Phase 3 trials in their EMERGENT program, evaluating KarXT for the treatment of psychosis in adults with schizophrenia, are enrolling. They also initiated their Phase 3 ARISE trial of KarXT for the treatment of schizophrenia in adults who experience an inadequate response to current standard of care. Additional clinical milestones include data from Karuna's completed Phase 1b trial of KarXT in healthy elderly volunteers, which Karuna intends to support a Phase 3 program evaluating KarXT for the treatment of psychosis in Alzheimer's disease, initiating in mid-2022. Earlier in 2021, results from the Phase 2 EMERGENT-1 trial evaluating KarXT for the treatment of schizophrenia were published in NEJM. Finally, Karuna announced entry into an exclusive license agreement with Zai Lab for the development, manufacturing and commercialization of KarXT in Greater China, including mainland China, Hong Kong, Macau and Taiwan. Karuna received a $35.0 million upfront payment and is eligible to receive certain development and regulatory milestone and sales milestone payments, as well as royalties based on annual net sales of KarXT in Greater China.
- **Akili:** Delivered strong progress on multiple fronts, including taking a step towards becoming a publicly-traded company. In the January 2022 post-period, Akili entered into a definitive agreement to become publicly traded via a merger with Social Capital Suvretta Holdings Corp. I (Nasdaq: DNAA), a special purpose acquisition company. With a fully committed PIPE of $162 million, transaction is expected to close in mid-2022, after which Akili will be listed on the Nasdaq stock market under the new ticker symbol "AKLI". Akili previously completed a $160 million financing, a new licensing agreement with Australian digital health company, TALi®, and the launch of new gaming features and functionalities for its FDA and European marketing-authorized video game treatment, EndeavorRx®, designed for children with attention deficit hyperactivity disorder (ADHD). Additionally, Akili initiated pilot studies of AKL-T01 for COVID brain fog in collaboration with Weill Cornell Medicine, New York Presbyterian Hospital and Vanderbilt University Medical Center. Akili also published data in *Nature Digital Medicine* from their STARS Adjunct study of EndeavorRx and announced positive results from Japanese partner Shionogi's Phase 2 ADHD study of SDT-001.

- **Gelesis (NYSE: GLS):** Made broad commercialization-focused progress in the U.S. toward the launch of Plenity®, an FDA-cleared weight management approach, for adults meeting prescription criteria. In the January 2022 post-period, Gelesis debuted as a public company following a business combination with Capstar Special Purpose Acquisition Corp., raising approximately $105 million in gross proceeds to support Plenity's launch. Also in the January 2022 post-period, Gelesis launched the "Who Said?" multichannel marketing campaign across the U.S., which challenges many long-held cultural and societal assumptions around weight loss. Other achievements include completing and validating its first commercial-scale manufacturing line, the successful LIGHT-UP study of GS200 in adults who are overweight or obese who also have prediabetes or type 2 diabetes and receipt of $40 million fully paid pre-orders for Plenity® from leading U.S. direct-to-patient healthcare company Ro. Finally, leading nutrition authority, Joy Bauer, MS, RDN, CDN, was appointed Chief Nutrition Officer of Plenity.
- **Vor Bio (Nasdaq: VOR):** Initiated VBP101, a Phase 1/2a clinical trial for VOR33, its eHSC therapy candidate for acute myeloid leukemia, an indication for which FDA granted Fast Track designation. Vor Bio also completed its initial public offering on Nasdaq under the ticker symbol "VOR", with gross proceeds of over $200 million. Additionally, Vor Bio entered into a collaboration with Janssen Biotech to investigate the combination of Vor Bio's "invisible" eHSC transplant platform with one of Janssen's bi-specific antibodies in development for AML.
- **Vedanta Biosciences:** Successfully completed its most advanced clinical study to date, achieving its primary endpoint in a Phase 2 clinical trial of VE303 for the prevention of recurrent CDI in high-risk patients. This triggered the exercise of a $23.8 million option by program partner, the U.S. Biomedical Advanced Research and Development Authority (BARDA), to support a Phase 3 clinical trial of VE303. Vedanta also completed a $68 million financing, including a $25 million investment from Pfizer as part of the Pfizer Breakthrough Growth Initiative.
- **Follica:** Appointed two leaders in aesthetic medicine and dermatology to its Board of Directors. Tom Wiggans, former Chief Executive Officer of Dermira, joined as Executive Chairman with over 30 years of experience leading biopharmaceutical companies from the start-up stage to global commercialization, and Michael Davin, former Chief Executive Officer of Cynosure, joined as an Independent Director with over 30 years of experience in the medical device industry.
- **Sonde:** Launched Sonde Mental Fitness, a voice-enabled mental health detection and monitoring technology that uses a brief voice journal entry to evaluate mental well-being, expanding Sonde beyond respiratory health. This news followed Sonde's collaboration announcement with leading chipmaker, Qualcomm Technologies, to embed Sonde's vocal biomarker technology on the flagship and high-tier Qualcomm® Snapdragon™ mobile platforms. This is intended to help bring native, machine learning-driven vocal biomarker capabilities to mobile and IoT devices globally.
- **Entrega:** Entrega's platform for the oral administration of biologics has continued development including via a partnership with Eli Lilly regarding certain Lilly therapeutic candidates.

We are well-positioned for a new stage of PureTech's development. In the year ahead, our anticipated catalysts continue to grow in scope and maturity, with two commercial entities – Gelesis and Akili – aiming to build launch momentum in addition to a wide range of clinical readouts and clinical pipeline expansion across the broader portfolio.

As always, I am proud of the breadth of activity and momentum PureTech sustains across our deep pipeline & portfolio, and am very grateful for the continued efforts, passion and counsel of our team, our R&D Committee and broader advisory network, as well as our Board and investors. Thank you to all. I am encouraged by the entrepreneurial spirit that is infused in our work and the mission that unites us in striving to bring powerful new medicines to patients.

To the patients and physicians taking part in our clinical trials: Thank you for your sacrifices and your trust in us as we work towards dramatically improving treatment for the conditions that impact your lives and the lives of many others. Advancing medicine is a shared project and we are privileged to partner with you in shaping its future.

Daphne Zohar
Founder, Chief Executive Officer and Director

April 25, 2022

Letter from the Chief Scientific Officer, Chief Medical Officer and Chief Innovation and Strategy Officer

"A year of advances in every aspect of PureTech R&D."

Joseph Bolen, Ph.D.,
Chief Scientific Officer

Julie Krop, M.D.,
Chief Medical Officer

Eric Elenko, Ph.D.,
Chief Innovation and Strategy Officer

2021 was a year of growth for PureTech's internal R&D as we significantly expanded our clinical activity across our Wholly Owned Pipeline while also delivering substantial research advances for our platform technologies. Our R&D strategy continues to support our overarching corporate focus on building a differentiated, integrated biopharmaceutical company focused on developing new therapies for underserved and often devastating diseases with limited or no options available for patients. Our unique innovative research engine is designed to produce new medicines that can be rapidly advanced into the clinic with our experienced fully integrated clinical, regulatory and manufacturing expertise.

Our research process begins by identifying therapeutic products for serious diseases that have a well-established human efficacy, but their usage is significantly limited by challenges, such as poor safety, tolerability, oral bioavailability or dosing.

Second, we apply our innovative research and development expertise and proprietary platform technologies, to these products to generate a novel therapeutic candidate that addresses one or more of the key underlying limitations and potentially unlock the full therapeutic effectiveness of the therapy.

The essential ingredient in our program selection is typically oriented around providing key benefits to the patients, such as substantially improving the tolerability profile of existing therapies that had previously demonstrated robust efficacy or through targeting of existing therapies to certain cells, such as the immune cells and sites of disease, such as inflammation, in order to improve efficacy while reducing systemic side effects.

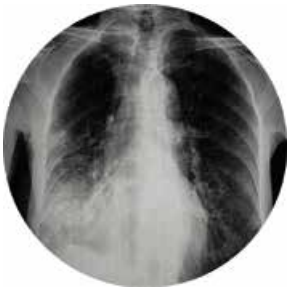
This strategy has helped us provide a solid foundation for PureTech's long-term growth. In addition to the success of our Founded Entity programs, we've also made tremendous strides with our Wholly Owned Pipeline, which is built on three potentially disruptive technology platforms in addition to external programs thematically identified to align with our immune modulation focus. We currently have seven therapeutic candidates in our Wholly Owned Pipeline including one that is being advanced as a partnered program. In 2021, we advanced three clinical-stage wholly-owned therapeutic candidates that have the potential to treat a range of indications including serious lung conditions, solid tumors lymphatic flow disorders and neurological indications. Additionally, we saw continued validation of our lymphatic and inflammation-focused technology platforms, including the advancement of a therapeutic candidate from one of these platforms into human studies and the achievement of preclinical proof-of-concept from another. The highlights of our extensive progress across the portfolio are summarized below:

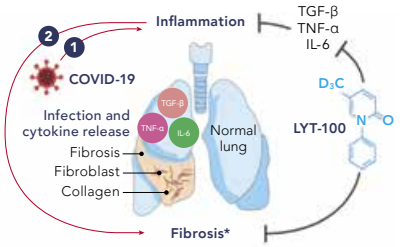
Multi-pronged progress for LYT-100 across a range of indications

LYT-100 (deupirfenidone) is our most advanced wholly-owned therapeutic candidate. It is a selectively deuterated form of pirfenidone, a drug that is approved for treating IPF, a serious and progressive lung disease. Based on prior work with pirfenidone, a substantial amount of preclinical and clinical data support LYT-100's broader potential in inflammatory and fibrotic conditions. These include lung disease (IPF and other respiratory conditions), and disorders of lymphatic flow, such as lymphedema. We are also exploring the potential evaluation of LYT-100 in radiation induced fibrosis, myocardial fibrosis and other organ system fibrosis. Due to LYT-100's broad potential across a range of fibrotic and inflammatory diseases, we expect LYT-100 to have a "pipeline within a product" opportunity which enables rapid clinical development in multiple indications, and so our clinical development strategy has focused on a comprehensive analysis of the potential applicability of

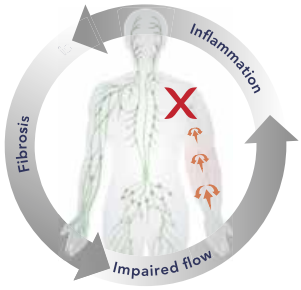
LYT-100 development plan overview

LYT-100-ILD	LYT-100-COV	LYT-100-LYMPH
Initiating registration-enabling studies in IPF in 1H 2022	Topline results expected from Phase 2 in Long COVID[1] in 1H 2022	Topline results expected from Phase 2a POC in lymphedema in 2022





*Fibrosis leads to chronic lung scarring and respiratory dysfunction, persisting post-discharge.



LYT-100 in areas of greatest unmet medical need that map against its known validated biological effects.

Although pirfenidone is one of the standard of care medicines for IPF and has demonstrated efficacy against this progressive, fatal disease, its usage has been greatly limited by the drug's severe tolerability issues – especially with regards to GI side-effects. Approximately half of the IPF patients that start therapy with pirfenidone either discontinue therapy, reduce their dose or switch to other therapies, all of which lead to suboptimal disease management. These issues pushed our team to establish a goal: To demonstrate a favorable tolerability profile of LYT-100 that could improve compliance and potentially lead to improved disease outcomes.

LYT-100's deuterium modification improves the metabolic stability of the molecule and enables its administration at a dosage that can achieve the same level of drug exposure as pirfenidone, but with a lower maximal drug concentration (Cmax). High Cmax is often associated with AEs, therefore by reducing the Cmax while maintaining the comparable exposure to pirfenidone, LYT-100 has the potential to allow the patient to stay on the therapy longer to potentially achieve an optimal therapeutic outcome.

To date, our clinical studies strongly support a substantial tolerability advantage of LYT-100 over pirfenidone. Our study enrolling healthy older adults showed an approximate 50% reduction in the number of healthy older adults treated with LYT-100 that experienced GI-related AEs relative to those treated with pirfenidone. Additionally, our multiple ascending dose study and our healthy older adults crossover study demonstrated that LYT-100 was well-tolerated at all doses studied and that all treatment-related AEs were mild and transient. Results of the Phase 1 multiple ascending dose and food effect study were presented at the virtual European Respiratory Society International Congress and published in the journal *Clinical Pharmacology in Drug Development*.

We attribute this improved tolerability to LYT-100's substantially differentiated PK properties that reduce AEs while preserving exposure and pharmacology. These results are extremely encouraging, and we are advancing LYT-100 into further clinical development for IPF.

Last year, we initiated a LYT-100 Phase 2 clinical study focused on patients who suffer from Long COVID respiratory complications. Since then, the pandemic has affected more than 500 million people around the world. Over 40% of hospitalized COVID-19 patients have lasting dyspnea and up to 33% of severe COVID-19 patients develop lung fibrosis. In the last 12 months, we've progressed the Phase 2 clinical trial of LYT-100 in patients who suffer from Long COVID respiratory complications and related sequelae, and we anticipate topline results in the first half of 2022.

We've also progressed LYT-100 in a Phase 2a proof-of-concept trial in patients with breast cancer-related, upper limb, secondary lymphedema. There are no approved treatments for lymphedema and we believe leveraging our unique insights into the lymphatic system and immunology can provide a role for deupirfenidone to make an impact for patients living with severe unmet medical need with this condition. Our preclinical work supports this hypothesis. In fact, in those studies, LYT-100 showed greater anti-fibrotic and anti-inflammatory activity when compared to pirfenidone. Results from the Phase 2a study are anticipated in 2022.

Anti-cancer programs: LYT-200 targeting galectin-9 and LYT-210 targeting gamma delta-1 T cells

Our anti-cancer programs target emerging, foundational immunosuppressive mechanisms to pursue a differentiated approach to cancer types that currently do not have adequate effective treatments. We see potential for PureTech as a leader against these targets, with both our fully human monoclonal antibody candidates having potential both as single agents and in combination with existing therapies such as checkpoint inhibitors and chemotherapeutics.

We are developing LYT-200 for solid tumors with currently poor survival rates. In 2021, the FDA granted LYT-200 orphan drug designation for the treatment of pancreatic cancer, which qualifies PureTech for incentives under the Orphan Drug Act, including tax credits for some clinical trials and eligibility for seven years of market exclusivity in the U.S. if the drug is approved, in addition to our broad intellectual property coverage which can extend the exclusivity into 2038.

1 Long COVID is a term being used to describe the emerging and persistent complications following the resolution of COVID-19 infection, also known as post-acute COVID-19 syndrome (PACS).

The ongoing Phase 1 portion of its adaptive Phase 1/2 study in solid tumors continues to progress, with a maximum tolerated dose not yet reached, and is expected to read out in the first half of 2022.

In 2021 we also began a clinical relationship with BeiGene to evaluate LYT-200 together with tislelizumab, an anti-PD-1 immune checkpoint inhibitor, in patients with solid tumors. LYT-200 is being evaluated as a single agent in the first phase of the adaptive Phase 1/2 study, which, pending the results, is then designed to investigate LYT-200 in combination with tislelizumab. While we believe that LYT-200 has the potential to have activity on its own, its mechanism for targeting immunosuppression may also lead to increased efficacy when combined with other cancer immunotherapies, such as checkpoint inhibitors or chemotherapeutic drugs, depending on the cancer.

For LYT-210, we presented promising preclinical data at the eminent American Association for Cancer Research (AACR) Annual Meeting. That research demonstrated that LYT-210 is both very specific and exceptionally potent, rapidly inducing cell death of immunomodulatory gamma delta-1 T cells, while sparing other T cells, such as cytotoxic gamma delta T cells, that play important roles in a healthy immune response. Gamma delta T cells are an increasingly well recognized approach for tackling difficult-to-treat cancers.

LYT-300: Harnessing lymphatic targeting through our Glyph™ platform

We were thrilled to initiate first-in-human clinical studies of LYT-300 (oral allopregnanolone) in December 2021. LYT-300 is the first candidate from the Glyph technology platform to enter the clinic, leveraging the platform's ability to enable direct delivery of an oral drug to the lymphatic system.

Given the research supporting the broad potential neurological and neuropsychological effects of allopregnanolone, LYT-300 is being evaluated for the potential treatment of a variety of conditions. The Phase 1 study evaluates multiple aspects of safety, tolerability and PK, and topline results are expected in the second half of 2022.

In early 2021, we presented preclinical proof-of-concept data for LYT-300 at the American College of Neuropsychopharmacology (ACNP) Annual Meeting.

As we advance LYT-300, we see its maturing data set as also being supportive of our Glyph technology platform. The Glyph technology enables us to generate novel prodrugs by reversibly linking small molecule drugs to dietary fat molecules. This linkage is designed to enable the transport of the small molecules directly into systemic circulation via the lymphatic system following oral administration, thereby bypassing first-pass liver metabolism.

We believe our Glyph platform could similarly enhance the potential of natural biologically active molecules or existing therapies that had previously demonstrated robust efficacy but could not be administered orally, by unlocking oral administration including natural neurosteroids or immune modulators that could directly target the mesenteric lymph nodes. Furthermore, preclinical proof-of-concept studies were published in the *Journal of Controlled Release* and *Nature Metabolism* that support the Glyph platform's ability to directly target the lymphatic system.

LYT-510, LYT-500, LYT-503/IMB-150: The integration of Alivio™

In 2021, we completed the acquisition of Alivio Therapeutics and the integration of its targeted anti-inflammatory platform technology and candidates into our Wholly Owned Pipeline. LYT-510, in development for the treatment of IBD and chronic pouchitis, is an oral inflammation-targeting formulation of tacrolimus. Tacrolimus is a potent immunosuppressant drug approved for certain indications, however its approval for IBD and chronic pouchitis has been hampered by systemic toxicities, narrow therapeutic window of activity and opportunistic infections that can arise from systemic immunosuppression. There is clinical data demonstrating that tacrolimus is effective in addressing IBD indications, but AEs have held it back. We believe that LYT-510 can overcome these clinical challenges with targeted drug delivery to the intestines, with the potential to be the first tacrolimus treatment approved for IBD in the U.S. We intend to file for regulatory approval to initiate first-in-human studies at year end 2022 and initiate a clinical study evaluating LYT-510 as a single agent for the potential treatment of IBD and chronic pouchitis in early 2023. LYT-500, an oral therapeutic candidate in development for the potential treatment of mucosal barrier damage in people with IBD, includes two orally dosed active agents (IL-22 and an immunosuppressant drug) designed to selectively act at inflamed intestinal tissues while reducing their impact on normal tissue. We expect preclinical proof-of-concept data for LYT-500 in the first half of 2022. We believe the targeted activation and oral formulation offered by Alivio offers a path to unlocking the full therapeutic potential of tacrolimus and other anti-inflammatory drugs in a way that matches the chronic, variable expression of autoimmune diseases.

The Alivio integration also includes the addition of therapeutic candidate, LYT-503/IMB-150, to our Wholly Owned Pipeline. It is being developed as a partnered program as a potential non-opioid treatment for interstitial cystitis or bladder pain syndrome (IC/BPS). An IND application is expected to be filed for LYT-503/IMB-150 in 2022.

Progressing the Orasome™ platform and other oral delivery technologies, and Meningeal Lymphatics Research Program

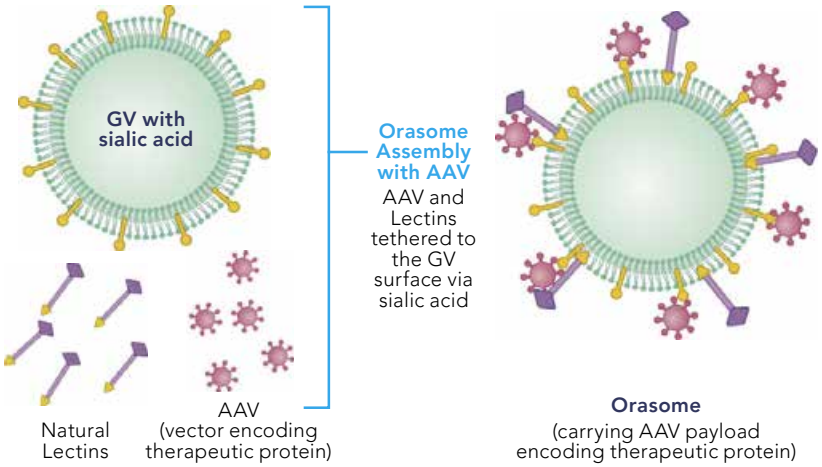
In addition to Glyph and Alivio, we are also making strides with the oral administration of biologics, such as the Orasome platform, and meningeal lymphatics research program. Each of these possesses a huge breadth of potential applications that could offer our pipeline many developmental options as they mature.

In 2021, the Orasome platform achieved preclinical proof-of-concept of its core concept: This technology is designed to promote following oral administration of an expression system, intestinal tract cells to produce virtually any type of therapeutic protein, including monoclonal antibodies, "on command" with transport to the circulatory system. We recently demonstrated in a preclinical model that administration of Orasomes carrying an expression system for a therapeutic protein, to the GI tract of a rodent led to therapeutic protein detection in systemic circulation.

This is a big idea – if we are successful, a patient could swallow a pill and have the body make its own therapeutic protein. We intend to generate additional preclinical data for Orasome and other technologies in 2022.

For our meningeal lymphatics research program, we and our collaborators published notable preclinical work in *Nature* suggesting that restoring lymphatic flow in the brain has the potential to address a range of neurodegenerative diseases, such as Alzheimer's and Parkinson's diseases and associated neuroinflammation. The research also uncovered a link between dysfunctional meningeal lymphatics and damaging microglia activation in Alzheimer's disease, suggesting another route by which restoring healthy (lymphatic) drainage could improve clinical outcomes.

Orasome Construct for oral administration of Therapeutic Proteins



AAV = Adeno Associated Virus; GV = Glycocalyx Vesicles

PureTech advantages: strategy, people and passion

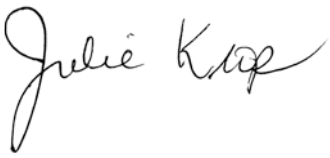
With many teams in the industry advancing single platform technologies, internally we are energized by the opportunity to be advancing a portfolio of programs across multiple promising approaches. They are built on leading research from our scientific collaborators and provide important innovative approaches that leverage validated biology and pharmacology to reduce technology and development risk. This is a key part of our R&D strategy, and we believe we realize synergies from their parallel internal development that potentially enable new medicines to advance.

Our approach gives PureTech multiple opportunities for success and we're proud of our track record, having now generated 27 therapeutics and therapeutic candidates, of which 16 are clinical stage and two have gone from inception through successful FDA and EU regulatory clearances for marketing.

To reach this point, we have collaborated with the world's leading domain experts on disease-specific discovery themes, particularly to leverage our expertise in immunology. All of our Wholly Owned Programs are building upon validated biologic pathways and proven pharmacology of known therapeutics while applying important innovation that enable new medicines to advance. We have proven our ability to utilize cross-disciplinary research and discovery efforts across multiple indications and potential therapeutic area thanks to a team of esteemed collaborators and co-inventors.

We are very proud of our work to advance our Wholly Owned Programs in 2021. Our focus on unmet medical needs in devastating diseases is a clear guiding principle that we believe brings out the best of our team and collaborators – we extend our warmest thanks to both for their efforts and counsel. We are in a transformative phase for PureTech and look forward to sharing our progress with you soon.

Dr. Joseph Bolen
Chief Scientific Officer



Dr. Julie Krop
Chief Medical Officer

Dr. Eric Elenko
Chief Innovation and Strategy Officer

April 25, 2022

How PureTech is building value for investors

"In light of the strong foundation we have built for PureTech's future growth, the Board and senior leadership team are considering various approaches to drive additional value to our shareholders. We are reviewing a capital allocation strategy that will see us prioritize funding the continued development and expansion of our Wholly Owned Pipeline and strategic investment in our Founded Entities in accordance with our strategic plan while we will also look to return certain proceeds we may receive in the future to shareholders through various distribution mechanisms, including share buybacks or special dividends."

We are a clinical-stage biotherapeutics company dedicated to discovering, developing and commercializing highly differentiated medicines for devastating diseases where limited or no treatment options currently exist for patients. We do this by building upon underlying mechanisms from well-established science that have been validated in clinical testing, while applying innovative insight or technology that generates new medicines that can unleash the full potential of the therapeutic. All the activity within our Wholly Owned Pipeline and the foundational activities at our Founded Entities were initiated by our experienced research and development team and our extensive network of scientists, clinicians and industry leaders. We are led by a proven and seasoned management team with significant experience in discovering and developing important new medicines, delivering them to market and maximizing shareholder value. Collectively, the members of our management team have overseen research and development of therapeutics supporting 26 regulatory approvals and have served in the C-suite of companies acquired for more than $14 billion in the aggregate.

Our model leverages collaboration with the world's leading experts in specific diseases, bringing together cross-disciplinary perspectives on new treatment opportunities. We combine these insights with our research and development expertise and proprietary platform technologies to generate novel therapeutic candidates that often are aimed at addressing key limitations with existing treatments that have limited their broad application or adoption. In addition to building on validated biology and clinical pharmacology, we further de-risk programs with key experiments at an early stage to validate the underlying value proposition. This model has enabled our consistent early access to scientific breakthroughs before their peer-reviewed publication and gives us an edge in advancing innovative and substantially differentiated treatment approaches for a range of indications including inflammatory, fibrotic and immunological conditions, intractable cancers, lymphatic and gastrointestinal diseases and neurological and neuropsychological disorders, among others.

Across the entire portfolio, we established the underlying programs and platforms that have resulted in 27 therapeutics and therapeutic candidates that are being advanced within our Wholly Owned Programs or by our Founded Entities. Of these therapeutics and therapeutic candidates, 16 are clinical-stage and two have been cleared for marketing by the FDA and granted marketing authorization in the European Economic Area, or EEA, and in other countries that recognize the CE Mark. Our publicly-listed Founded Entities, Karuna, Vor and Gelesis, are advancing seven of these therapeutic candidates, including two that are currently in Phase 3/Pivotal studies, as well as one FDA-cleared therapeutic. Our privately-held Founded Entities, Akili, Vedanta, Follica, Sonde and Entrega, are advancing 13 other therapeutic candidates, including two that are expected to enter a Phase 3 study. Finally, we are advancing seven therapeutic candidates within our Wholly Owned Pipeline, including one therapeutic candidate that is being as a partnered program, with two Phase 2 and two Phase 1 clinical trials underway. We and our Founded Entities have relationships with several pharmaceutical companies or their investment arms to advance some of the programs and platforms underlying these therapeutics and therapeutic candidates.

This diverse portfolio is a natural result of the innovative R&D model we pioneered for therapeutic development. It adds stability to our anticipated growth trajectory and feeds value back into the core enterprise centered on the Wholly Owned Programs. The basis for our high growth strategy is to build a differentiated, integrated biopharmaceutical company that develops its own therapeutics while also benefiting from the successes of the now-independent Founded Entities. This provides PureTech with a strong foundation for sustainable growth with a well-managed risk profile that helps drive new opportunities for patients as well as shareholder value.

Components of our Value

The table to the right depicts the four components of our value: **(1)** our Wholly Owned Programs, **(2)** Founded Entities, **(3)** our available cash, cash equivalents and short-term investments at the PureTech level and **(4)** our return of capital to shareholders.

We hold majority voting control of or otherwise retain significant influence over our Controlled Founded Entities and continue to play a role in the development of their therapeutic candidates through representation on their boards of directors. Our board designees represent a majority of the members of the board of directors of Follica and Vedanta and a minority of the members of the board of directors of Sonde and Entrega. With respect to our Non-Controlled Founded Entities, we do not hold majority equity ownership and are not responsible for the development or commercialization of their therapeutic candidates and therapeutics. Our Non-Controlled Founded Entities have independent management teams, and we do not control the day-to-day development of their respective therapeutic candidates.

1. **Our Wholly Owned Programs.** We are focused on the advancement of our Wholly Owned Programs and delivering value to our shareholders by driving our Wholly Owned Programs to key clinical and commercial milestones, while continuing cutting-edge research and development efforts to discover and advance new therapeutic candidates. The table to the right includes a summary of our Wholly Owned Programs and their development status.
2. **Our Founded Entities**[1]**.** The table to the right summarizes the therapeutic candidates being developed by our Founded Entities in order of our equity value. We established the underlying programs and platforms that have resulted in the therapeutic candidates noted in the table, each of which targets indications related to one or more of the brain, immune and gastrointestinal systems, and advanced them through key validation points. In certain cases, our interest in the therapeutic candidates of these entities is limited to the potential appreciation of our equity interest in these entities. In other cases, we have an equity interest in these entities and the right to receive royalty payments on product sales and/or sublicense revenues. Any value we realize from these therapeutic candidates will be through the potential growth and realization of equity and royalty stakes, including sublicense payments from pharma partnerships entered into with certain Founded Entities.
3. **Cash and Cash Equivalents.** We had PureTech Level Cash and Cash Equivalents of $418.9 million as of December 31, 2021[2].
4. **Our Return of Capital to Shareholders.** In light of the strong foundation we have built for PureTech's future growth, the Board and senior leadership team are considering various approaches to drive additional value to our shareholders. We are reviewing a capital allocation strategy that will see us prioritize funding the continued development and expansion of our Wholly Owned Pipeline and strategic investment in our Founded Entities in accordance with our strategic plan while we will also look to return certain proceeds we may receive in the future to shareholders through various distribution mechanisms, including share buybacks or special dividends.

1 While PureTech maintains ownership of equity interests in its Founded Entities, the Company does not, in all cases, maintain control over these entities (by virtue of (i) majority voting control and (ii) the right to elect representation to the entities' boards of directors) or direct the management and development efforts for these entities. Consequently, not all such entities are consolidated in the Company's financial statements.

2 For more information in relation to the PureTech Level Cash and Cash Equivalents and Consolidated Cash and Cash Equivalents measures used in this Annual Report, please see pages 97 and 98 of the Financial Review.

3 The FDA and corresponding regulatory authorities will ultimately review our clinical results and determine whether our wholly-owned therapeutic candidates are safe and effective. No regulatory agency has made any such determination that our wholly-owned therapeutic candidates are safe or effective for use by the general public for any indication. On July 23, 2021, Imbrium Therapeutics exercised its option to license LYT-503/IMB-150 pursuant to which it is responsible for all future development activities and funding for LYT-503/IMB-150.

4 Long COVID is a term being used to describe the emerging and persistent complications following the resolution of COVID-19 infection, also known as post-acute COVID-19 syndrome (PACS).

5 Relevant ownership interests and references to equity ownership for Founded Entities contained in this strategic report (pages 2-72) were calculated on a partially diluted basis (as opposed to a voting basis) as of December 31, 2021, including outstanding shares, options and warrants, but excluding unallocated shares authorized to be issued pursuant to equity incentive plans. Vor, Karuna and Gelesis ownerships were calculated on a beneficial ownership basis in accordance with SEC rules as of March 4, 2022 and February 15, 2022 and March 31, 2022, respectively.

6 With the exception of Plenity® and EndeavorRx®, candidates are investigational and have not been cleared by the FDA for use in the U.S.

7 PureTech has a right to royalty payments, including sublicense payments, as a percentage of net sales.

8 Please see footnote 10 on page 6 for EndeavorRx® indication and overview.

9 These therapeutic candidates are regulated as devices and their development has been approximately equated to phases of clinical development.

10 Please see footnote 11 on page 7 for Important Safety Information about Plenity®.

1 Wholly Owned Programs

Our Programs[3]	Discovery	Preclinical	Phase 1	Phase 2	Phase 3
LYT-100-ILD Deupirfenidone	IPF				
LYT-100-COV Deupirfenidone	Long COVID[4] respiratory complications and related sequelae				
LYT-100-LYMPH Deupirfenidone	Lymphatic flow disorders, including lymphedema				
LYT-200 Anti-Galectin-9 mAb	Solid tumors				
LYT-210 Anti-Delta-1 mAb	Solid tumors				
LYT-300 Oral Allopregnanolone	Neurological and neuropsychological conditions				
LYT-510 Oral Immunosuppressant	IBD/chronic pouchitis				
LYT-500 Oral IL-22 + Immunosuppressant	IBD				
LYT-503/IMB-150 (Partnered program) Non-opioid	IC/BPS				

Registration-enabling studies to begin in 1H2022 | Phase in progress | Phase completed

Lymphatic and Inflammation Platforms

- Glyph™ Technology Platform (Lymphatic Targeting)
- Orasome™ and Other Technology Platforms (Oral Biotherapeutics)
- Alivio™ Technology Platform (Inflammation Targeting)
- Meningeal Lymphatics Research Program

2 Founded Entities

Founded Entity	PureTech Ownership[5]	Therapeutic Candidate[6]		Indication	Stage of Development	Royalties[7]
KARUNA THERAPEUTICS	5.6%	KarXT	P	Schizophrenia Alzheimer's disease psychosis	Phase 3 Phase 3 Ready	Royalties
AKILI	22.3%	Akili is pioneering the development of cognitive treatments through game-changing technologies. EndeavorRx®[8] (formerly known as AKL-T01) is the first FDA cleared and CE marked video game treatment. In the U.S., EndeavorRx is indicated to improve attention function as measured by computer-based testing in children ages 8-12 years old with primarily inattentive or combined-type ADHD, who have a demonstrated attention issue.				
GELESIS	23.5%	Plenity®[9,10] Plenity® for adolescents[9] GS200[9] GS300[9] GS500[9]	D D D D	Weight management Adolescent weight management Weight management in T2D/prediabetes NASH/NAFLD Functional constipation	Commercial Pending Discussion with FDA Clinical Trial Complete Clinical Pivotal	Royalties
VOR	8.6%	VOR33 (CD33) VCAR33	B B	Acute myeloid leukemia Myelodysplastic syndromes, myeloproliferative neoplasms Bridge-to-transplant AML	Phase 1/2a Preclinical Phase 1/2	N/A
VEDANTA BIOSCIENCES	41.4%	VE303 VE202 VE416 VE800 VE707	B B B B B	*C. difficile* IBD Food allergy Solid tumors Gram-negative infections	Phase 3 Ready Phase 2 Ready Phase 1/2 Phase 1 Preclinical	N/A
follica	76.0%	FOL-004	P/D	Androgenetic alopecia	Phase 3 Ready	Royalties
SONDE	44.6%	Sonde One for Respiratory[9] Sonde Mental Fitness[9]	D D	Respiratory risk detection and monitoring app Monitoring vocal features linked to depression, anxiety, and cognition	Commercial Release Commercial Release	N/A
entrega	74.3%	ENT-100	B	Oral delivery of biologics, vaccines and other drugs	Preclinical	N/A

The letters next to the therapeutic candidates denote whether the therapeutic candidate is a pharmaceutical product (P), biologic (B) or device (D).

3 PureTech Level Cash and Cash Equivalents as of December 31, 2021: $418.9m[2]

4 Our Return of Capital to Shareholders

Key Pipeline Components and Expected Milestones Through 2022

Through 2022, we anticipate many significant potential milestones across our Wholly Owned Programs and Founded Entities, including at least 10 clinical readouts, at least five clinical trial initiations and the full commercial rollout of two therapeutics. Of these, five clinical readouts and one clinical trial initiation are anticipated within our Wholly Owned Pipeline. Additionally, we expect the continued progress of discovery and preclinical programs, as well as the potential for additional strategic partnerships and transactions and the growth of value through our equity and royalty holdings in our Founded Entities. Our Wholly Owned Programs and certain of our Founded Entities' programs that contribute to our value are as follows:

Our Wholly Owned Programs Focused on Immunological, Fibrotic and Lymphatic System Disorders:

LYT-100, Our Lead Clinical-Stage Therapeutic Candidate Targeting a Range of Conditions Involving Inflammation and Fibrosis and Disorders of Lymphatic Flow: We are advancing our clinical-stage therapeutic candidate LYT-100 (deupirfenidone) for the potential treatment of conditions involving inflammation and fibrosis, including lung disease (IPF and Long COVID[11] respiratory complications and related sequelae) and disorders of lymphatic flow, such as lymphedema. We are also exploring the potential evaluation of LYT-100 in other inflammatory and fibrotic conditions such as radiation induced fibrosis, myocardial fibrosis and other organ system fibrosis based on the strength of existing clinical data around the use of pirfenidone in these indications. In the January 2022 post-period, we announced results from a randomized, double-blind crossover study in healthy older adults demonstrating that approximately 50% fewer subjects treated with LYT-100 experienced GI-related AEs compared to subjects treated with pirfenidone (17.4% vs. 34.0%). Based on these results, additional data generated from our robust LYT-100 clinical program and recent regulatory feedback, we intend to advance LYT-100 into late-stage clinical development for the treatment of IPF, streamlining the program by capitalizing on efficiencies of the 505(b)(2) regulatory pathway. The dose-ranging study, which is anticipated to begin in the first half of 2022, will enroll approximately 250 treatment-naïve patients to evaluate LYT-100 efficacy relative to placebo. The trial will also compare the relative tolerability and efficacy between LYT-100 and pirfenidone. Topline results from this study are expected by the end of 2023. We believe the results of this study, together with a Phase 3 study, could serve as the basis for registration in the U.S. Additionally, two Phase 2 clinical trials of LYT-100 progressed in 2021: 1) A Phase 2 trial of LYT-100-COV in adults with Long COVID respiratory complications and related sequelae. Topline results from this trial are expected in the first half of 2022. 2) A Phase 2a proof-of-concept study of LYT-100-LYMPH in patients with breast cancer-related, upper limb secondary lymphedema. Topline results from this trial are expected in 2022. In 2021, we initiated a three-month, open-label extension of the LYT-100-COV Phase 2 trial in adults with Long COVID respiratory complications and related sequelae who completed the first portion of the trial. The primary endpoint of the extension trial will measure change in distance walked on the 6MWT, with secondary endpoints to assess the longer-term safety and tolerability of LYT-100-COV through up to 182 days of treatment. We also initiated additional Phase 1 clinical trials in 2021 to further evaluate the PK, dosing and tolerability of LYT-100 in healthy volunteers and healthy older adults to inform the clinical development of LYT-100 across multiple indications. Results from these studies demonstrated that LYT-100 was well-tolerated at 824mg TID dosing with low rates of GI AEs that were comparable to placebo. These results will further inform our dose-ranging study design in treatment-naïve IPF patients. In April 2021, we announced the formation of a Clinical Advisory Board for IPF and other PF-ILDs. In August 2021, we presented the results of the Phase 1 multiple ascending dose and food effect study of LYT-100 at the virtual European Respiratory Society (ERS) International Congress. The results from the study were subsequently published in the journal *Clinical Pharmacology in Drug Development* in November 2021.

LYT-200 and LYT-210, Two Immuno-Oncology (IO) Therapeutic Candidates Harnessing Key Immune Cell Trafficking and Programming Mechanisms: The lymphatic system plays a crucial role in programming immune cells for precise functions and trafficking them to specific tissues. By modulating immune cell trafficking and programming, we are developing therapeutic candidates for the potential treatment of cancer and other immunological disorders. We are advancing LYT-200, targeting a foundational immunosuppressive protein, galectin-9, for the potential treatment of difficult-to-treat solid tumors including pancreatic ductal adenocarcinoma (PDAC), colorectal cancer (CRC) and cholangiocarcinoma (CCA), and LYT-210, targeting immunomodulatory gamma delta-1 T cells for a range of cancer indications. LYT-200 is being evaluated as a single agent in the first stage of an adaptive Phase 1/2 clinical trial. The primary objective of the Phase 1 portion of the trial is to assess the safety and tolerability of escalating doses of LYT-200 to identify a dose to carry forward into the Phase 2 portion of the trial. The Phase 1 portion will also assess the PK and pharmacodynamic (PD) profiles of LYT-200. Topline results from the Phase 1 portion of the study are anticipated in the first half of 2022. Pending these results, we intend to initiate the Phase 2 expansion cohort portion of the trial, which is designed to evaluate LYT-200 both as a single agent and in combination with chemotherapy or BeiGene's tislelizumab, an anti-PD-1 mAb for which we and an affiliate of BeiGene, Ltd. entered into a clinical trial and supply agreement in July 2021. Under the terms of the agreement, we will maintain control of the LYT-200 program, including global R&D and commercial rights, and BeiGene has agreed to supply tislelizumab for use in combination with LYT-200 for the planned Phase 2 study cohorts. In November 2021, the FDA granted orphan drug designation to LYT-200 for the treatment of pancreatic cancer. The FDA grants orphan drug designation to novel drug and biologic products for the treatment, diagnosis or prevention of conditions affecting fewer than 200,000 persons in the U.S. Orphan Drug designation qualifies PureTech for incentives under the Orphan Drug Act, including tax credits for some clinical trials and eligibility for seven years of market exclusivity in the U.S. if the drug is approved, in addition to our broad intellectual property coverage which can extend the exclusivity into 2038. In April 2021, we presented a scientific poster detailing additional promising preclinical results for LYT-210 at the 2021 American Association for Cancer Research (AACR) Annual Virtual Meeting. The research demonstrated that LYT-210 is both highly specific

11 Long COVID is a term being used to describe the emerging and persistent complications following the resolution of COVID-19 infection, also known as post-acute COVID-19 syndrome (PACS).

and highly potent, rapidly inducing cell death of immunomodulatory gamma delta-1 T cells, while sparing other T cells that play important roles in a healthy immune response. We expect to complete additional biomarker studies for LYT-210 in 2022.

LYT-300, Preclinical Therapeutic Candidate Developed Using our Glyph Technology Platform, Targeting Neurological and Neuropsychological Conditions: Using our Glyph platform, which harnesses the natural trafficking of dietary lipids via the lymphatics, we are advancing LYT-300, an oral form of allopregnanolone, for the potential treatment for a range of neurological and neuropsychological conditions. Allopregnanolone is a natural neurosteroid that is a positive allosteric modulator of γ-aminobutyric-acid type A ($GABA_A$) receptors, which are known to play a key biological role in depression, epilepsy and other neurological and neuropsychological conditions. In December 2021, we initiated a Phase 1 clinical study of LYT-300, which is designed to characterize the safety, tolerability and PK of orally administered LYT-300 in healthy volunteers. Results are expected in the second half of 2022 and will be used to inform the design of possible future studies evaluating LYT-300 in indications that could include depression, anxiety, sleep disorders, fragile X tremor-associated syndrome, essential tremor and epileptic disorders, among others. Also in December 2021, we presented preclinical proof-of-concept data at the 60th American College of Neuropsychopharmacology (ACNP) Annual Meeting supporting the clinical advancement of LYT-300. The data presented at ACNP showed that systemic exposure of natural allopregnanolone was achieved after oral administration of LYT-300 in multiple preclinical models of increasing complexity. In contrast, systemic levels of allopregnanolone were not observed following oral administration of natural unmodified allopregnanolone. These results demonstrate the potential of the Glyph technology platform to enhance the systemic absorption of natural bioactive molecules and other small molecules with poor oral bioavailability. We are also advancing our Glyph technology platform, which is designed to employ the lymphatic system's natural lipid absorption and transport process and has led to the nomination of a new therapeutic candidate, LYT-300, for continued expansion of our Wholly Owned Pipeline. We have successfully extended the platform to encompass more than 20 molecules as well as a range of novel linker chemistries that have demonstrated promising lymphatic targeting in preclinical studies. In 2021, preclinical proof-of-concept work was published in *Nature Metabolism* and the *Journal of Controlled Release* supporting the Glyph technology platform's ability to directly target the lymphatic system.

LYT-510, LYT-500 and LYT-503/IMB-150, our Therapeutic Candidates Developed Using our Alivio Technology Platform for Inflammatory Disorders: In June 2021, we announced the acquisition of the remaining 22% of shares outstanding in our Founded Entity, Alivio Therapeutics (Alivio). The underlying Alivio technology platform, which is designed to enable oral and locally targeted immunomodulation for the potential treatment of a range of chronic and acute inflammatory disorders, has been added to our lymphatic and inflammation programs. Alivio's therapeutic candidates, in development for inflammatory disorders including IBD, have also been integrated into our Wholly Owned Pipeline. The first of these candidates is LYT-510, an oral inflammation-targeting formulation of tacrolimus, a potent immunosuppressant drug, in development to treat IBD and chronic pouchitis. In multiple preclinical IBD models, LYT-510 showed significant improvements in several efficacy endpoints compared to untreated controls. Furthermore, the inflammation-targeting properties were shown to result in very low systemic blood levels compared to the current immunosuppressant formulations, which minimizes the potential for systemic side effects. We intend to file for regulatory approval to initiate first-in-human studies at year end 2022 and initiate a clinical study evaluating LYT-510 as a single agent for the potential treatment of IBD and chronic pouchitis in early 2023. In addition, LYT-500 is an orally-administered therapeutic candidate in development for the treatment of IBD that contains a unique combination of IL-22 and an approved potent anti-inflammatory drug and is designed to address the key underlying causes of IBD pathogenesis and progression, such as mucosal barrier disruption that are currently not adequately treated by the standard of care medicines. We expect preclinical proof-of-concept data for LYT-500 in the first half of 2022. LYT-503/IMB-150 is a therapeutic candidate being advanced as a partnered program for the potential treatment of IC/BPS, a chronic inflammatory condition of the bladder that lacks an effective treatment option. The LYT-503/IMB-150 therapeutic candidate is designed to selectively treat inflamed tissues along the bladder wall while minimizing the potential for drug-related side effects in healthy parts of the body. An IND application is expected to be filed for LYT-503/IMB-150 in 2022.

In addition to our Glyph and Alivio lymphatic and inflammation platforms, our Wholly Owned Programs include Orasome and other oral biotherapeutics platforms enabling the body to produce its own therapeutic protein in the gastrointestinal tract and enter the systemic circulation via the lymphatic system – and a meningeal lymphatics research program to develop potential treatments for neurodegenerative and neuroinflammatory diseases.

Orasome and Other Technology Platforms for Oral Administration of Therapeutics: We are developing versatile and programmable oral biotherapeutics approaches, such as our Orasome technology, to promote following oral administration of an expression system, intestinal tract cells, to produce virtually any type of therapeutic protein, including monoclonal antibodies, "on command" with transport to the circulatory system. We recently demonstrated in a preclinical model that administration of Orasomes carrying an expression system for a therapeutic protein to the GI tract of a rodent led to therapeutic protein detection in systemic circulation. In 2021, we established preclinical proof-of-concept supporting the potential of the Orasome technology platform to achieve production of therapeutic proteins in the gut of an animal following simulated oral administration of expression systems and transport of these proteins from the gut into systemic circulation. Proof-of-concept was observed with multiple formulations which are being further optimized to achieve a range of expression profiles for therapeutic proteins. We expect to generate additional data in 2022, with Orasomes and other technologies, across a range of preclinical models and therapeutic proteins. We expect to generate data to demonstrate that oral administration of Orasomes, carrying an expression system for a desired therapeutic protein, can achieve therapeutic levels of the protein in multiple species of preclinical models with achievement of safe repeat-dose administration. Using the Orasome technology platform, it may be possible for a patient to take an oral drug product that will permit their own GI tract cells to make virtually any type of protein. This approach also has the potential to provide a more convenient and significantly less expensive means to administer biological medicines. This work could lay the foundation for IND-enabling clinical studies for one or more additional therapeutic candidates to be included in our Wholly Owned Pipeline. In addition to Orasomes, we are also exploring the use of other approaches, such as certain exosomes isolated from milk as well as synthetic novel polymers and vesicles for delivering biotherapeutics.

Our Meningeal Lymphatics Research Program: We continued to advance our meningeal lymphatics research program, which harnesses the meningeal lymphatics to potentially treat a range of neurodegenerative and neuroinflammatory conditions. In April 2021, we announced the publication of preclinical research in *Nature*, suggesting that restoring lymphatic flow in the brain, either alone or in combination with passive immunotherapies such as antibodies directed at amyloid-beta, has the potential to address a range of neurodegenerative diseases, such as Alzheimer's and Parkinson's diseases, which potentially impairs the efficacy of passive immunotherapies such as amyloid-beta-targeting antibodies. The work also uncovered a link between dysfunctional meningeal lymphatics and damaging microglia activation in Alzheimer's disease, suggesting another route by which restoring healthy drainage patterns could improve clinical outcomes.

Founded Entities

Karuna

Karuna Therapeutics, Inc., or Karuna, which is developing its novel therapies with the potential to deliver transformative medicines for people living with psychiatric and neurological conditions, made progress towards developing KarXT (xanomeline-trospium), an oral, investigational M1/M4-preferring muscarinic acetylcholine receptor agonist in development for the treatment of psychiatric and neurological conditions, including schizophrenia and psychosis in Alzheimer's disease (AD). KarXT is designed to unlock the therapeutic potential of xanomeline, which demonstrated significant benefits in reducing symptoms of psychosis in Phase 2 studies in schizophrenia and AD, while ameliorating side effects seen in earlier studies. In August 2021, Karuna announced that all four Phase 3 trials in the EMERGENT program, the clinical program evaluating KarXT for the treatment of psychosis in adults with schizophrenia, are enrolling. In November 2021, Karuna announced that topline data from EMERGENT-2, a five-week inpatient trial evaluating the efficacy and safety of KarXT compared to placebo in 246 adults with schizophrenia in the U.S., are expected in mid-2022. EMERGENT-3, a five-week inpatient trial evaluating the efficacy and safety of KarXT compared to placebo in 246 adults with schizophrenia in the U.S. and Ukraine, is underway. EMERGENT-4, a 52-week outpatient, open-label extension trial evaluating the long-term safety and tolerability of KarXT in 350 adults with schizophrenia who completed EMERGENT-2 or EMERGENT-3, and EMERGENT-5, a 52-week outpatient, open-label trial evaluating the long-term safety and tolerability of KarXT in adults with schizophrenia who were not enrolled in EMERGENT-2 or EMERGENT-3, are also underway. Enrollment for this trial began in the second quarter of 2021. Karuna plans to increase the number of sites in the U.S. and Puerto Rico, and allow for up to 600 patients in the trial. In June 2021, Karuna announced data from its completed Phase 1b trial evaluating the safety and tolerability of KarXT in healthy elderly volunteers, which followed a preliminary analysis of data from the first two cohorts in the trial announced earlier in 2021. The results suggest that KarXT can be administered to elderly volunteers at doses which achieve xanomeline blood levels similar to those reported in the Phase 2 EMERGENT-1 trial in adults with schizophrenia while maintaining a favorable tolerability profile. Data from the trial also suggest that a lower dose ratio of trospium to xanomeline, compared to the ratios used in Phase 1 trials in healthy adult volunteers and in the Phase 2 EMERGENT-1 trial evaluating KarXT in adults with schizophrenia, was better tolerated by healthy elderly volunteers. Based on results from the Phase 1b trial in healthy elderly volunteers, Karuna plans to initiate a Phase 3 program evaluating KarXT for the treatment of psychosis in AD in mid-2022, with details available in the first half of 2022. In November 2021, Karuna announced the evaluation of KarXT for the treatment of dementia-related psychosis (DRP) will initially focus on psychosis in AD, the most common subtype of DRP. The initial focus on the AD dementia subtype reflects various strategic development, regulatory and commercial considerations, and Karuna remains interested in exploring KarXT in other dementia subtypes in future development programs. In November 2021, Karuna initiated the Phase 3, six-week, 1:1 randomized, double-blind, placebo-controlled ARISE trial evaluating KarXT for the treatment of schizophrenia in approximately 400 adults who experience an inadequate response to current standard of care. Participants in this trial will continue their currently prescribed atypical antipsychotic therapy at the same dose or regimen schedule as prior to entry in the study, and will receive a flexible dose of KarXT or placebo based on tolerability and clinical response as determined by a clinician. In late 2021, Karuna initiated a Phase 1 trial of an advanced formulation of KarXT as it continued to advance its earlier pipeline of muscarinic receptor targeted programs and novel formulations of KarXT. Karuna is also advancing its artificial intelligence-based target agnostic discovery program for treating psychiatric and neurological conditions. Karuna also continues to advance its earlier pipeline of muscarinic receptor targeted programs and novel formulations of KarXT, including its artificial intelligence-based target agnostic discovery program for treating psychiatric and neurological conditions. Additionally, in November 2021, Karuna and Zai Lab (Shanghai) Co., Ltd. (Zai) announced their entry into an exclusive license agreement for the development, manufacturing, and commercialization of KarXT in Greater China, including mainland China, Hong Kong, Macau and Taiwan. Under the terms of the agreement, Karuna received a $35.0 million upfront payment and is eligible to receive certain development and regulatory milestone and sales milestone payments, as well as royalties based on annual net sales of KarXT in Greater China. Zai Lab will fund substantially all development, regulatory and commercialization activities in Greater China. In February 2021, Karuna announced that results from the Phase 2 EMERGENT-1 trial evaluating KarXT for the treatment of schizophrenia were published in NEJM. In March 2021, Karuna completed a follow-on public offering of its common stock, from which it received net proceeds of $270.0 million. In 2021, we sold 1,750,000 shares of Karuna common stock for cash consideration of approximately $218 million in two separate transactions in February and November. We intend to use the proceeds from the transaction to further expand and advance its clinical-stage Wholly Owned Pipeline. We are eligible to receive certain sublicense payments and royalties on sales of any commercialized product covered by the license agreement between us and Karuna pursuant to the terms of such license agreement. Our interest in Karuna also includes our equity ownership of 5.6% at February 15, 2022.

Akili

Akili Interactive Labs, Inc., or Akili, has made progress in advancing its digital diagnostics, treatments and monitors for cognitive impairments across disease and disorders. In the January 2022 post-period, Akili entered into a definitive agreement to become publicly traded via a merger with Social Capital Suvretta Holdings Corp. I (Nasdaq: DNAA), a special purpose acquisition company. The transaction is expected to close in mid-2022, after which Akili will be listed on the Nasdaq stock market under the new ticker symbol "AKLI". The transaction implies a post-money equity value of the combined company of up to approximately $1 billion and is expected to deliver up to $412 million in gross cash proceeds to Akili, including the contribution of up to $250 million of cash held in SCS's trust account and $162 million from PIPE investors at $10 per share. In May 2021, Akili closed on the $160 million combined equity and debt financing, which is expected to accelerate commercialization of EndeavorRx®[12]. In March 2021, the full data from a multi-site open-label study (the STARS Adjunct study) evaluating the impact of EndeavorRx (AKL-T01) on symptoms and functional impairments in children with attention-deficit/hyperactivity disorder (ADHD) was published in *Nature Digital Medicine*. In the February 2022 post-period, Akili announced the publication of full data in the medical journal *PLOS ONE* from a single arm, unblinded study conducted by Dr. Elysa Marco at Cortica Healthcare and Drs. Joaquin Anguera and Courtney Gallen at the University of California, San Francisco. The study measured electroencephalography (EEG) data alongside behavioral and clinical metrics of attention in children with ADHD using AKL-T01 (EndeavorRx). Data from the study show that EndeavorRx treatment resulted in increased brain activity related to attention function, as measured by EEG, which correlated with improvements in objective behavioral measures of attention. In September 2021, Akili announced topline results from Shionogi's Phase 2 study of SDT-001 (Japanese version of AKL-T01) that showed treatment was well-received by patients and demonstrated improvements in attention-deficit/hyperactivity disorder (ADHD) inattention symptoms consistent with those seen across previous studies of AKL-T01. In July 2021, Akili introduced new gaming features and functionalities to its EndeavorRx treatment. Akili is releasing these new gameplay features as it expands its pre-launch activities to bring EndeavorRx to families and healthcare professionals. In April 2021, Akili announced collaborations with Weill Cornell Medicine, New York-Presbyterian Hospital and Vanderbilt University Medical Center to initiate pilot studies of Akili digital therapeutic AKL-T01 as a treatment for patients with cognitive dysfunction following COVID-19 (also known as "COVID fog"). In August 2021, Akili and Australian digital health company TALi (ASX:TD1), completed an agreement for Akili to license TALi's technology designed to address early childhood attention impairments. Our interest in Akili is limited to our equity ownership of 22.3% at December 31, 2021.

Gelesis

Gelesis Holdings, Inc., or Gelesis, has continued to advance its novel category of treatments for weight management and gut related chronic diseases. In December 2021, Gelesis announced its lead product, Plenity[13] (formerly known as Gelesis100), is now broadly available in the U.S. to adults who meet the prescription criteria. In the January 2022 post-period, Gelesis announced the completion of its business combination with Capstar Special Purpose Acquisition Corp. (NYSE: CPSR) ("Capstar"). Gelesis Holdings, Inc. began trading on the New York Stock Exchange under the ticker symbol "GLS" on January 14, 2022. In the January 2022 post-period, Gelesis launched the "Who Said?" marketing campaign across the U.S., which challenges many long-held cultural and societal assumptions around weight loss. Plenity's multichannel campaign encompasses TV, digital, social and Out of Home (OOH) to grow awareness of Plenity's novel approach to weight management. In the March 2022 post-period, Gelesis announced preliminary results from its broad awareness media campaign, noting that within the first three weeks, Gelesis saw a 3-fold increase in web traffic and 3.5-fold increase in the number of individuals seeking a new prescription compared to previous months when supply was limited. In November 2021, Gelesis announced that it had received a $30 million fully paid pre-order, in addition to the $10 million pre-order received in January 2021, for Plenity from Ro, a leading U.S. direct-to-patient healthcare company. Plenity was initially made available through a beta launch in 2020, and demand quickly outpaced supply while Gelesis worked to construct a larger manufacturing facility. Gelesis' first commercial-scale manufacturing line at the facility was also completed and validated in November 2021. In late 2021, Gelesis completed a preliminary analysis of the LIGHT-UP study, a multicenter, randomized, double-blind, placebo-controlled, investigational study that enrolled 254 subjects with overweight or obesity who also have prediabetes or type 2 diabetes, and that analysis remains underway. The study was designed to assess the change in body weight in adults after six months of treatment with a new oral superabsorbent hydrogel (GS200) or placebo. The study met both of its primary endpoints: the proportion of participants who achieved at least 5% body weight loss (defined as "Responders") and the change in body weight as compared to placebo after six months of therapy. The LIGHT-UP study was conducted at 36 clinical sites in Europe and North America with 208 subjects who completed the 6-month study. In November 2021, Gelesis announced a publication in Nature's *Scientific Reports* describing the genesis of the underlying technology and engineering process for Gelesis' non-systemic superabsorbent hydrogels. These new materials were designed to replicate compositional and mechanical properties of raw vegetables, and the paper describes their therapeutic approach for weight management as well as possible future solutions for other gut-related conditions. In May 2021, Gelesis presented a scientific poster at the American Association of Clinical Endocrinology (AACE) 2021 Annual Virtual Meeting. The post-hoc analysis showed that treatment for weight management with Plenity decreased a marker for liver fibrosis (the NAFLD fibrosis score) compared to placebo. We are eligible to receive certain payments from Gelesis under our license agreement, including sublicense payments and royalties on any sales of Plenity. Our interest in Gelesis also includes our equity ownership of 23.5% at March 31, 2022.

12 Please see footnote 10 on page 6 for EndeavorRx® indication and overview.
13 Please see footnote 11 on page 7 for Important Safety Information about Plenity®.

Vor

Vor Bio, Inc. or Vor, a clinical-stage cell and genome engineering company that aims to change the standard of care for patients with blood cancers by engineering hematopoietic stem cells (HSC) to enable targeted therapies post-transplant, continued to engineer eHSC therapies combined with targeted therapies for the treatment of cancer in 2021. In February 2021, Vor Bio completed its initial public offering of common stock on the Nasdaq Global Market under the symbol "VOR". The aggregate gross proceeds to Vor Bio from the offering were approximately $203.4 million, before deducting the underwriting discounts and commissions and other offering expenses payable by Vor Bio. In the March 2022 post-period, Vor Bio announced VCAR33 is now made up of two programs with different cell sources. The VCAR33 programs are chimeric antigen receptor T (CAR-T) cell therapy candidates designed to target CD33, a clinically-validated target for AML. VCAR33^{AUTO} uses autologous cells from each patient, and is being studied in an ongoing Phase 1/2 clinical trial sponsored by the National Marrow Donor Program (NMDP) in young adult and pediatric patients with relapsed/refractory AML in a bridge-to-transplant study. Data from this study are expected in 2022. VCAR33^{ALLO} uses allogeneic healthy donor-derived cells. Vor Bio plans to submit an IND application in the first half of 2023 to support a Phase 1/2 clinical trial of VCAR33^{ALLO} for patients with relapsed/refractory AML. Additionally, Vor Bio announced in the March 2022 post-period its plans to collect initial data on VOR33 from the VBP101 clinical trial and initial clinical data from the VCAR33^{ALLO} program prior to IND submission for the Treatment System following ongoing discussions with the FDA and alongside improved scientific understanding of the differences in T-cell sources. Vor Bio plans to share initial clinical data from the VBP101 trial of VOR33 for patients with AML in the second half of 2022. In September 2021, the FDA granted Fast Track designation to VOR33 for the treatment of acute myeloid leukemia (AML). Vor Bio initiated VBP101, a Phase 1/2a clinical trial of VOR33 for AML patients who currently have limited treatment options and expects to report VOR33's initial clinical data in the second half of 2022. Vor Bio also expects to submit an IND filing with the FDA for the VOR33/VCAR33 Treatment System in the second half of 2022. In November 2021, Vor Bio announced its first multi-targeted Treatment System comprising VOR33-CLL1 multiplex-edited eHSC therapy and VCAR33-CLL1 multi-specific CAR-T therapy and it continues to make progress on editing multiple antigens with its eHSC platform. Vor Bio plans to share preclinical data on its VOR33-CLL1 + VCAR33-CLL1 Treatment System approach at upcoming scientific meetings in 2022. Vor Bio expects initial monotherapy clinical proof-of-concept data for VCAR33 in 2022, depending on investigator's timing of data release. In June 2021, Vor Bio announced the build-out of an in-house clinical manufacturing facility in Cambridge, Massachusetts in the same premises as Vor Bio's current headquarters, to support flexible manufacturing for the company's eHSC and CAR-T product candidate pipeline for patients with blood cancers. Vor Bio anticipates that the facility will be operational in 2022. In July 2021, Vor Bio formed a collaboration with Janssen Biotech, Inc. (Janssen), one of the Janssen Pharmaceutical Companies of Johnson & Johnson to investigate the combination of Vor Bio's "invisible" eHSC transplant platform with one of Janssen's bi-specific antibodies in development for AML. In June 2021, Vor Bio entered into a multi-year strategic collaboration and license agreement with Abound Bio to research both single- and multi-targeted CAR-T treatments to be used in combination with Vor Bio's eHSC platform, with the goal of generating novel treatment systems for patients fighting AML and other devastating forms of blood cancer. Our interest in Vor Bio is limited to our equity ownership of 8.6% at March 4, 2022.

Vedanta

Vedanta Biosciences, Inc., or Vedanta, progressed the development of a potential new category of oral therapies based on defined consortia of bacteria is isolated from the human microbiome and grown from pure clonal cell banks. In October 2021, Vedanta announced that it achieved the primary endpoint in a Phase 2 clinical trial of VE303, an orally administered investigational live biotherapeutic product (LBP) in development for the prevention of recurrent *C. difficile* infection (CDI) in high-risk patients. Based on the Phase 2 data, the Biomedical Advanced Research and Development Authority (BARDA) exercised its first contract option for additional funding of $23.8 million, pursuant to its existing 2020 contract with Vedanta, to support a planned Phase 3 clinical trial of VE303. In July 2021, Vedanta closed a $68 million financing, which included a $25 million investment from Pfizer as part of the Pfizer Breakthrough Growth Initiative. Vedanta plans to use the proceeds to advance its pipeline of defined bacterial consortia, including progressing VE303 into a Phase 3 clinical trial in patients at high risk for recurrent CDI, initiating a Phase 2 clinical trial of VE202 in mild to moderate ulcerative colitis. In late 2021, Vedanta completed the build-out of its Phase 3 and commercial launch CGMP manufacturing facility for supply of VE303. In June 2021, Vedanta presented additional results from a Phase 1 study in healthy volunteers of VE202 for IBD at the 2021 International Human Microbiome Consortium Congress (IHMC). In July 2021, Vedanta announced results from the Phase 1 study evaluating the safety and initial clinical activity of VE800, an immuno-oncology therapeutic candidate, in combination with Bristol Myers Squibb's Opdivo® (nivolumab) in 54 patients across select types of advanced or metastatic cancers. Vedanta plans to present the results at a future medical conference and will continue work to identify cancer settings and patient populations that might benefit from microbiome manipulation with its defined bacterial consortia. Our interest in Vedanta is limited to our equity ownership of 41.4% at December 31, 2021.

Follica

Follica, Incorporated, or Follica, continued to advance its regenerative platform designed to treat androgenetic alopecia, epithelial aging and other related conditions. In January 2021, Follica announced the appointment of two leaders in aesthetic medicine and dermatology to its Board of Directors. Follica continued to advance its regenerative biology platform, including preparing for a registration clinical program in male androgenetic alopecia, which is expected to be initiated in 2022. Follica also has proprietary amplification compounds in development and ongoing discovery efforts to expand its pipeline. We are eligible to receive certain payments from Follica under our license agreement, including sublicense payments and royalties on any sales of certain potential products by Follica. Our interest in Follica also includes our equity ownership of 76.0% at December 31, 2021.

Sonde

Sonde Health, Inc. or Sonde, continued the development of its proprietary voice-based technology platform designed to detect changes of health conditions – like mental fitness and respiratory disease – from changes in voice, leveraging over one million voice samples from 80,000+ individuals. In October 2021, Sonde launched Sonde Mental Fitness, a voice-enabled mental health detection and monitoring technology that uses a brief voice sample to evaluate mental well-being. Sonde Mental Fitness is available as an application programming interface for health systems, employers and wellness services. Sonde One, its health screening app, helps large organizations to execute a daily population screening regimen that can help reduce the spread of COVID-19, comply with government mandates and return to work safely. In the January 2022 post-period, Sonde announced the signing of a multi-year strategic partnership with GN Group to research and develop commercial vocal biomarkers for mild cognitive impairment. The research will serve as the backbone for new voice-based tools to help at-risk individuals gain timely and accurate health insights using GN Group's device technologies and, ultimately, to enable early detection and management of life-threatening diseases for the millions of people living with hearing loss. In July 2021, Sonde announced a strategic collaboration with leading chipmaker, Qualcomm, to embed Sonde's vocal biomarker technology on the flagship and high-tier Qualcomm® Snapdragon™ 888 and 778G 5G Mobile Platforms to help bring native, machine learning-driven vocal biomarker capabilities to mobile and IoT devices globally. Sonde plans to launch key pilot programs in the employer wellness, health system and provider space in 2022. Our interest in Sonde is limited to our equity ownership of 44.6% at December 31, 2021.

Entrega

Entrega, Inc. or Entrega, advanced its platform for the oral administration of biologics, vaccines and other drugs that are otherwise not efficiently absorbed when taken orally. As part of its collaboration with Eli Lilly, Entrega has continued to investigate the application of its peptide administration technology to certain Eli Lilly therapeutic candidates. The partnership has been extended into 2022. Entrega has also continued advancement of its ENT-100 platform for the oral administration of biologics, vaccines and other drugs that are otherwise not efficiently absorbed when taken orally. Our interest in Entrega is limited to our equity ownership of 74.3% at December 31, 2021.

Our Mission: Developing Breakthrough Medicines for Underserved and Serious Diseases

The programs within our Wholly Owned Programs and at our Founded Entities were initiated in close collaboration with leading academic and clinical experts. We discover, develop and aim to commercialize new therapies for underserved and often devastating diseases where limited or no treatment options currently exist for patients. We do this by building upon validated biology of known therapeutics while applying unique innovative steps that improve pharmacologic profiles.

Unlocking the Potential of Validated Biology

The common theme underlying all of our programs has been to start with a tremendous patient need. In many cases, these programs are identified based on signals of human efficacy and clinically validated biology, which has enabled us to advance therapeutic candidates with significantly de-risked profiles and robust development rationales, resulting in differentiated potential treatments for patients.

For example, the key innovation behind our Founded Entity, Karuna, was built around two validated drugs: xanomeline, a novel muscarinic agonist, and trospium, an approved muscarinic antagonist. We were able to ameliorate the GI tolerability issues of xanomeline by pairing it with a gut-restricted muscarinic antagonist to develop a novel formulation that enabled a new approach for the potential treatment of schizophrenia and other serious psychiatric and neurological conditions, an area of major unmet need. KarXT now represents a potential first-in-class and best-in-class therapy for schizophrenia.

We have continued to harness the power of this approach to develop new medicines by applying our innovation and technology that can unleash the full potential of a therapeutic that was previously held back from their full potential by key challenges, such as poor safety, tolerability, oral bioavailability or dosing.

LYT-100

Pirfenidone has been proven effective against fibrosis and inflammation, but significant tolerability issues negatively affect patient compliance and often result in suboptimal disease management. To tackle this problem, we are developing a proprietary clinical-stage therapeutic candidate, LYT-100 (selectively deuterated form of pirfenidone) that maintains the pharmacology of pirfenidone but has a highly differentiated PK profile that has translated into favorable tolerability, as demonstrated by data from multiple human clinical studies.

LYT-300/Glyph™ Technology Platform

Allopregnanolone is a natural neurosteroid with well-established biology that has demonstrated efficacy for the treatment of epilepsy, depression and other neurological indications. However, it is not orally bioavailable and is commercially formulated to be administered as a cumbersome 60-hour IV infusion. We have applied our innovative Glyph technology to generate LYT-300, which is an orally bioavailable prodrug of natural allopregnanolone. Our Glyph technology platform is based on the natural process of dietary lipid transport in the body. We use the Glyph technology to design prodrugs of natural bioactive molecules, such as allopregnanolone, for oral administration of drugs, that are transported via the lymphatic system and bypass first-pass liver metabolism. LYT-300 has been shown in preclinical models to enable allopregnanolone to be bioavailable.

LYT-510, LYT-500/Alivio™ Technology Platform

Our Alivio technology platform is designed to target biologics and other drugs to sites of inflammation in a localized manner while limiting their systemic exposure, which offers the potential to significantly improve both the safety and efficacy profile of the therapy. We are developing LYT-510 as an oral inflammation-targeting formulation of tacrolimus, a potent immunosuppressant drug, to treat IBD and chronic pouchitis. Tacrolimus is approved for certain indications, however its approval for IBD and chronic pouchitis has been hampered by systemic toxicities, narrow therapeutic window of activity and opportunistic infections that can arise from systemic immunosuppression. There is clinical data demonstrating that tacrolimus is effective in addressing IBD indications, but AEs have held it back. We believe that LYT-510 can overcome these clinical challenges with targeted drug delivery to the intestines, with the potential to be the first tacrolimus treatment approved for IBD in the U.S. In multiple preclinical IBD models, LYT-510 showed significant improvements in several efficacy endpoints compared to untreated controls. Furthermore, the inflammation-targeting properties were shown to result in very low systemic blood levels compared to the current immunosuppressant formulations, which minimizes the potential for systemic side effects. LYT-500 is an oral therapeutic candidate that we are developing for the potential treatment of mucosal barrier damage in people with IBD. We believe the targeted activation and oral formulation offered by Alivio offers a path to unlocking the full therapeutic potential of anti-inflammatory drugs in a way that matches the chronic, variable expression of autoimmune diseases.

Orasome™ and Other Technology Platforms for Oral Administration of Therapeutics

Validated biology has shown that intestinal cells can be engineered to produce clinically validated therapeutic proteins, such as EPO, GLP-1 and mAbs. Therapeutic proteins and nucleic acid therapeutics (e.g. mRNA) are primarily administered by injection. Using the Orasome technology platform, it may be possible for a patient to take an oral drug product that will permit their own gastrointestinal tract cells to make virtually any type of therapeutic protein. This approach also has the potential to provide a more convenient and significantly less expensive means to administer biological medicines. In addition to Orasomes, we are also exploring the use of other approaches, such as certain exosomes isolated from milk as well as synthetic novel polymers and vesicles for delivering biotherapeutics.

Our Model

We employ the following process to identify and develop therapeutic candidates:

- **Step 1: A Collaborative Discovery Process Leveraging Validated Biology and our Scientific Network:** We collaborate with the world's leading domain experts on a disease-specific discovery theme through our core areas of expertise around brain, immune and gastrointestinal systems, with a particular focus on immunological disorders. Our Wholly Owned Programs are built around this expertise and we prioritize programs that have the potential to reduce early development risk based on preliminary signals of activity in humans and promising tolerability profiles. We have proven our ability to efficiently leverage our cross-disciplinary research and discovery efforts across multiple indications and potential therapeutic areas. Our program collaborators and co-inventors across our Wholly Owned Programs and Founded Entities' programs include leading academic minds; recipients of major awards such as the Nobel Prize, the U.S. National Medal of Science, the Charles Stark Draper Prize and the Priestley Medal; members of prestigious institutions such as the Howard Hughes Medical Institute, all three of the National Academies and world-renowned academic institutions such as Harvard, MIT, Yale, Columbia, Johns Hopkins, Imperial College of London and Cornell, among others; and former senior executives and board members at some of the world's largest pharmaceutical companies.
- **Step 2: A Disciplined Approach to Program Advancement:** We employ a rigorous and disciplined approach to research and development. The breadth and depth of our Wholly Owned Programs and our Founded Entities' programs allow us to quickly pivot resources to the more promising therapeutic opportunities, strategically reallocate capital across programs and terminate Wholly Owned Programs we choose not to pursue without adversely impacting the development of other programs. Through our internal resources and with our extensive expert network and collaboration partners, we repeat key academic work and conduct focused experiments both internally and externally to rapidly advance those that we believe hold the greatest promise and deprioritize less attractive programs. Collectively, these activities decrease the risk of any individual program event negatively impacting our Wholly Owned Programs and enable us to preserve capital for the programs across our Wholly Owned Programs and Founded Entities that we believe have the greatest opportunity for value creation in alignment with our shareholders.
- **Step 3: A Capital Efficient Approach to Driving Clinical Development and Value Creation:** Our management team has successfully driven these therapeutic candidates from early-stage research and development, through POC and into clinical trials and has supported dedicated teams at our Non-Controlled Founded Entities through pivotal trials and FDA clearance. We have financed our development efforts through strategic collaborations, pharmaceutical partnerships, non-dilutive funding mechanisms, including through the sale of our Founded Entities' equity and through grants, and public and private equity financings. We leverage shared resources, institutional knowledge and infrastructure between our earlier stage Founded Entities and development efforts within our Wholly Owned Programs to advance our programs efficiently prior to POC. This approach has enabled the discovery and development of 27 therapeutics and therapeutic candidates to date, including two that have been cleared for marketing by the FDA and granted marketing authorization in the EEA, between our Wholly Owned Programs and our Founded Entities, in which we retain equity ownership ranging from 5.6% to 76.0%. We had PureTech Level Cash and Cash Equivalents of $418.9 million as of December 31, 2021[14]. From January 1, 2017 to December 31, 2021, our Founded Entities strengthened their collective balance sheets by attracting $1.9 billion in investments and non-dilutive funding, including $1.8 billion from third parties. As part of our disciplined capital management, we have been able to generate $578.0 million in non-dilutive funding, as of December 31, 2021, through the sales of portions of Founded Entity shares.

Our Strategy

Driving development of potential new medicines and accretion of value via three paths

1	**Advance Wholly Owned Programs through development and commercialization, including pipeline expansion**	**Wholly Owned Programs** LYT-100, LYT-200, LYT-210, LYT-300, LYT-510, LYT-500, LYT-503/IMB-150, Lymphatic and Inflammation Platforms
2	**Derive value from equity growth of Founded Entities** (e.g., M&A, IPO and sale of equity (($578 million as of December 31, 2021), royalties and sublicense payments)	**External Founded Entities** Gelesis, Karuna, Follica, Vedanta, Sonde, Entrega, Akili, Vor Bio
3	**Advance and de-risk discovery platforms by partnering non-core applications** via non-dilutive funding sources including partnerships and grants	**Non-core Applications of Wholly-Owned Discovery Platforms**

14 For more information in relation to the PureTech Level Cash and Cash Equivalents and Consolidated Cash and Cash Equivalents measures used in this Annual Report, please see pages 97 and 98 of the Financial Review.

15 On July 23, 2021, Imbrium Therapeutics exercised its option to license LYT-503/IMB-150 pursuant to which it is responsible for all future development activities and funding for LYT-503/IMB-150.

Our goal is to identify, invent, develop and commercialize innovative new categories of therapeutics that are derived from our deep understanding of the brain, immune, and gastrointestinal systems, with a particular focus on immunological disorders, to address significant unmet medical needs. To achieve this goal, key components of our strategy include:

- Advancing Wholly Owned Programs through development and commercialization, including pipeline expansion:
  - Progressing LYT-100, LYT-200, LYT-210, LYT-300, LYT-510, LYT-500, and LYT-503/IMB-150[15] through clinical studies.
  - Harnessing our proprietary drug discovery and development capabilities to drive pipeline maturation and expansion: We are pioneering the development of therapeutic candidates by leveraging our unique insights into the lymphatic system and immunology and drug development. Our Wholly Owned Programs currently comprise seven proprietary therapeutic candidates and three innovative technology platforms. We intend to leverage our proprietary lymphatic and inflammation technology platforms, as well as our extensive network with world-leading scientists in immunology and lymphatics and major pharmaceutical companies, to generate and acquire additional novel therapeutic candidates. To do so, we will rely on the track record of our team, which has been instrumental in the generation of 27 therapeutics and therapeutic candidates to date between our Wholly Owned Programs and our Founded Entities, including two that have been cleared for marketing by the FDA and granted marketing authorization in the EEA, as well as our established internal identification and prioritization approach. In many cases, these programs are identified based on signals of human efficacy and clinically validated biology, which has enabled us to advance candidates with significantly de-risked profiles and robust development rationales. We will continue to take advantage of our differentiated model to manage the risk of any single program and quickly redeploy resources towards performing assets.
  - Maximizing the impact of our Wholly Owned Programs by expanding development across multiple indications: We aim to focus our development efforts on therapeutic candidates that have the potential to treat multiple diseases and plan to develop them in additional indications where warranted. For example, we believe that our lead therapeutic candidate LYT-100 has the potential to treat multiple inflammatory and fibrotic indications that affect the lung, heart and other organ systems. We are initially developing our other therapeutic candidates, LYT-200 and LYT-210, for the treatment of difficult-to-treat solid tumors, which will likely include PDAC, CRC and CCA. We are advancing LYT-300, an oral lipid prodrug version of allopregnanolone generated from our Glyph platform, for the potential treatment of a range of neurological and neuropsychological conditions. Lastly, we are developing LYT-510 for the potential treatment of IBD and chronic pouchitis, LYT-500, an oral combination therapy, for the potential treatment of IBD, and advancing LYT-503/IMB-150 as a partnered program for the potential treatment of IC/BPS. Each therapeutic candidate was generated from our Alivio technology platform.
- Deriving value from equity growth of our Founded Entities: Going forward, our Founded Entities may participate in private and public financings, enter into partnerships and collaborations, partner with equity investors, pharmaceutical and biotechnology companies and government and non-governmental organizations and generate revenues from sales of products. We hold equity ownership in our Founded Entities and benefit from their growth and catalysts such as M&A transactions, IPOs and royalties from sales. We also intend to strategically monetize our equity holdings in our Founded Entities over time after significant value inflection has occurred, generating non-dilutive financing. For example, PureTech generated cash proceeds of approximately $218 million in 2021 from the sales of equity in our Founded Entities.
- Advancing discovery platforms by partnering non-core applications via non-dilutive funding sources, including partnerships and grants, to enable retention of value: As we further develop our Wholly Owned Programs through key value inflection points, we may opportunistically enter into strategic partnerships when we believe that such partnerships could add value to the development or potential commercialization of our wholly-owned therapeutic candidates. We will also continue to pursue government grant funding and discovery partnerships that allow us to maintain most of the value of our platforms while offsetting operational costs.

We believe this combination of development of our Wholly Owned Programs, Founded Entity advancement and non-dilutive partnerships and funding provides us with a unique and multi-pronged engine fueling potential future growth and a diverse portfolio of differentiated treatment opportunities for patients.

By Order of the Board

Daphne Zohar
Founder, Chief Executive Officer and Director

April 25, 2022

PureTech's Wholly Owned Programs

Our programs

Therapeutic Candidate[1]	Indication	Discovery	Preclinical	Phase 1	Phase 2	Phase 3
LYT-100-ILD Deupirfenidone	IPF					
LYT-100-COV Deupirfenidone	Long COVID[2] respiratory complications and related sequelae					
LYT-100-LYMPH Deupirfenidone	Lymphatic flow disorders, including lymphedema					
LYT-200 Anti-Galectin-9 mAb	Solid tumors					
LYT-210 Anti-Delta-1 mAb	Solid tumors					
LYT-300 Oral Allopregnanolone	Neurological and neuropsychological conditions					
LYT-510 Oral Immunosuppressant	IBD/chronic pouchitis					
LYT-500 Oral IL-22 + Immunosuppressant	IBD					
LYT-503/IMB-150 (Partnered program) Non-opioid	IC/BPS					

Phase completed Phase in progress Registration-enabling studies to begin in 1H2022

Our Head of Research, Anne Burkhardt, and her team works to advance our Wholly Owned Programs in our headquarters.

1 The FDA and corresponding regulatory authorities will ultimately review our clinical results and determine whether our wholly-owned therapeutic candidates are safe and effective. No regulatory agency has made any such determination that our wholly-owned therapeutic candidates are safe or effective for use by the general public for any indication.

2 Long COVID is a term being used to describe the emerging and persistent complications following the resolution of COVID-19 infection, also known as post-acute COVID-19 syndrome (PACS).

LYT-100

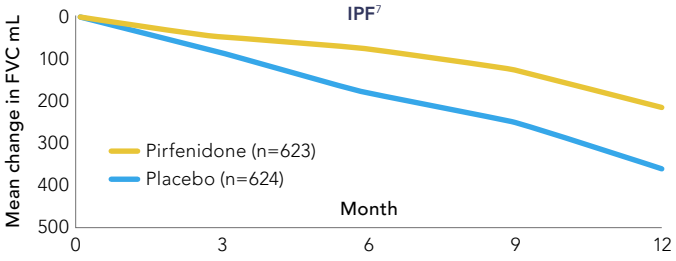
Therapeutic Candidate[1]	PureTech Ownership	Indication	Stage of Development
LYT-100	Wholly-owned	Idiopathic pulmonary fibrosis (IPF)	Registration-enabling studies planned
		Long COVID[2] respiratory complications and related sequelae	Phase 2
		Lymphatic flow disorders, including lymphedema	Phase 2
		Exploring potential opportunities in other inflammatory and fibrotic conditions, such as radiation induced fibrosis, myocardial fibrosis, and other organ system fibrosis	Clinical studies being planned

- Our lead wholly-owned therapeutic candidate, LYT-100 (deupirfenidone), is being advanced for the potential treatment of conditions involving inflammation and fibrosis, including lung disease (IPF and Long COVID respiratory complications and related sequelae) and disorders of lymphatic flow, such as lymphedema. We are also exploring the potential evaluation of LYT-100 in other inflammatory and fibrotic conditions, such as radiation induced fibrosis, myocardial fibrosis and other organ system fibrosis based on the strength of existing clinical data around the use of pirfenidone in these indications. LYT-100 is a selectively deuterated form of pirfenidone that is designed to retain the potent and clinically validated anti-fibrotic and anti-inflammatory activity of pirfenidone, but with a highly differentiated PK profile that has translated into favorable tolerability, as supported by data from multiple human clinical studies. To date, LYT-100 has been studied in more than 400 subjects and demonstrated a favorable safety profile as part of our ongoing development work and indication prioritization.

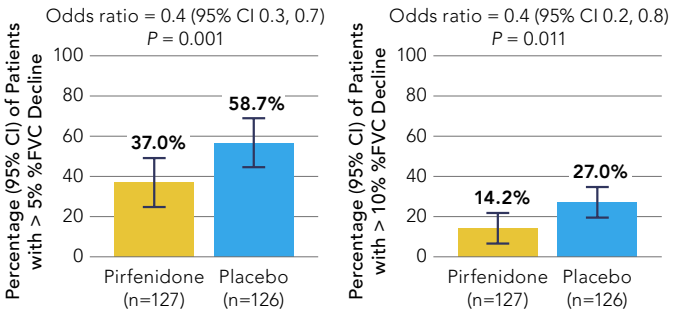
Key Points of Innovation & Differentiation

- Pirfenidone (Esbriet®[3]) slows the progression of IPF and has been approved for the treatment of IPF in the U.S. and other countries. IPF is a chronic orphan condition that causes progressive scarring of the lungs. Median overall survival of IPF patients is 3-5 years. Pirfenidone is one of the two standard of care treatments for IPF, with nintedanib (OFEV®[3]) being the other drug. Despite its proven efficacy, there are serious limitations to pirfenidone's clinical use primarily due to severe GI-related tolerability issues, which have significantly curtailed its effectiveness in patients with IPF[4]. The other standard of care treatment for IPF, nintedanib, has similar GI-related tolerability issues and limitations that have limited its broad usage. Although the combined sales of these two standard of care IPF drugs are over $3B, only about 25% of IPF patients are currently being treated with either of these drugs[5]. The vast majority of IPF patients are not currently on any approved therapies, primarily due to tolerability issues associated with these drugs. In a large post-marketing analysis of 10,996 patients diagnosed with IPF, only 13.2% received treatment with pirfenidone during a five-year follow-up period[6]. Additionally, real-world experience with pirfenidone in the IPF treatment setting highlights significant problems with treatment compliance, resulting in approximately half of the patients that start therapy either discontinuing therapy, dose-reducing or switching to other therapies, all of which lead to suboptimal disease management. We are developing LYT-100-ILD to offer an improved tolerability profile compared to current standard of care drugs, which may enable better patient compliance and potentially lead to improved disease outcomes. Pirfenidone has also shown activity in investigational clinical studies in patients with unclassifiable interstitial lung disease (uILD), radiation induced fibrosis, myocardial fibrosis and other organ system fibrosis and has demonstrated activity in a preclinical model of lymphedema and radiation-induced fibrosis.

Pirfenidone: Clinically Validated Anti-Fibrotic and Anti-Inflammatory



Unclassifiable Interstitial Lung Disease (uILD)[8]



- Pirfenidone FDA-approved for IPF with breakthrough designation for uILD
- Over a dozen late-stage & real-world efficacy studies demonstrate efficacy in IPF[9]
- Clinical proof-of-concept studies in FSGS, uILD, radiation-induced fibrosis & other inflammatory & fibrotic diseases
- BUT GI-related tolerability issues significantly limit its usage, resulting in ~50% who discontinue, dose adjust, or switch[10]
- ~75% of IPF patients are not on standard of care therapy[6]
- Despite drawbacks, pirfenidone sales >$1B / year

1 We have an active IND on file with the FDA for LYT-100. The FDA and corresponding regulatory authorities will ultimately review our clinical results and determine whether our wholly-owned therapeutic candidates are safe and effective. No regulatory agency has made any such determination that LYT-100 is safe or effective for use by the general public for any indication.

2 Long COVID is a term being used to describe the emerging and persistent complications following the resolution of COVID-19 infection, also known as post-acute COVID-19 syndrome (PACS).

3 Esbriet®, OFEV® and AUSTEDO® are trademarks of Genentech, Boehringer Ingelheim Pharmaceuticals and Auspex Pharmaceuticals, Inc., respectively, and are not owned by or affiliated with PureTech Health. LYT-100 is an investigational drug not approved by any regulatory authority.

4 Rubino C. M., Bhavnani S. M., Ambrose P. G., Forrest A., Loutit J. S. Effect of food and antacids on the pharmacokinetics of pirfenidone in older healthy adults. Pulmonary Pharmacology & Therapeutics. 2009 Aug;22(4):279-285. DOI: 10.1016/j.pupt.2009.03.003.

5 Based on 2021 ESBRIET® and OFEV® total WW sales of $3.7B; Ofev sales are inclusive of SSc-ILD, PF-ILD and IPF indications.

6 Dempsey TM, Payne S, Sangaralingham L, Yao X, Shah ND, Limper AH. Adoption of the Anti-Fibrotic Medications Pirfenidone and Nintedanib for Patients with Idiopathic Pulmonary Fibrosis. Ann Am Thorac Soc. 2021 Jan 19. doi: 10.1513/AnnalsATS.202007-901OC. Epub ahead of print. PMID: 33465323.

7 Noble, P. W., Albera, C., Bradford, W. Z., Costabel, U., du Bois, R. M., Fagan, E. A., Fishman, R. S., Glaspole, I., Glassberg, M. K., Lancaster, L., Lederer, D. J., Leff, J. A., Nathan, S. D., Pereira, C. A., Swigris, J. J., Valeyre, D., & King, T. E., Jr (2016). Pirfenidone for idiopathic pulmonary fibrosis: analysis of pooled data from three multinational phase 3 trials. The European Respiratory Journal, 47(1), 243–253. https://doi.org/10.1183/13993003.00026-2015.

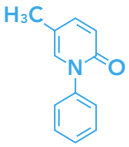
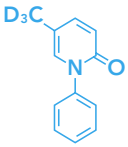
8 ERS 2019: http://bit.ly/2IJ9WCC

9 Saad, M. I., Mcleod, L., Hodges, C., Vlahos, R., Rose-John, S., Ruwanpura, S., & Jenkins, B. J. (2021). ADAM17 Deficiency Protects against Pulmonary Emphysema. American Journal of Respiratory Cell and Molecular Biology, 64(2), 183-195. doi:10.1165/rcmb.2020-0214oc.

10 Cottin, V., Koschel, D., Günther, A., Albera, C., Azuma, A., Sköld, C. M., Tomassetti, S., Hormel, P., Stauffer, J. L., Strombom, I., Kirchgaessler, K. U., Maher, T. M. (2018). Long-term safety of pirfenidone: Results of the prospective, observational PASSPORT study. ERJ Open Research, 4(4), 00084-2018. doi:10.1183/23120541.00084-2018.

Key Points of Innovation & Differentiation (continued)

- LYT-100 is a selectively deuterated form of pirfenidone that is designed to retain the potent and clinically-validated anti-fibrotic and anti-inflammatory activity of pirfenidone with a highly differentiated PK profile that has translated into favorable tolerability, as demonstrated by data from multiple human clinical studies.
- As recently demonstrated in a crossover study comparing LYT-100 to pirfenidone in healthy older adults, lower maximal LYT-100 drug concentration (Cmax) with exposure that is bioequivalent to pirfenidone was achieved. This is supportive of the observed improved tolerability.
- A PK profile of LYT-100 that is substantially better tolerated than pirfenidone while maintaining comparable efficacy has the potential to allow the patients to stay on the drug longer. As a result, we believe LYT-100-ILD has the potential to replace pirfenidone as standard of care and to become a backbone therapy in the treatment for IPF.

Pirfenidone	LYT-100
	
✔ Clinically validated efficacy ✗ Associated with GI AEs ✗ Higher exposure limited by tolerability	✔ Differentiated PK profile while retaining pharmacology ✔ Substantially improved AE profile ✔ Potential to enhance exposure that could improve efficacy, MTD not determined

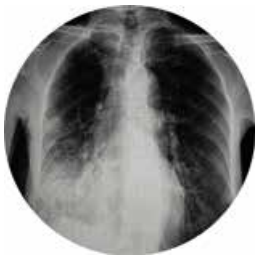
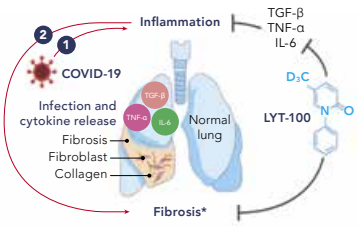
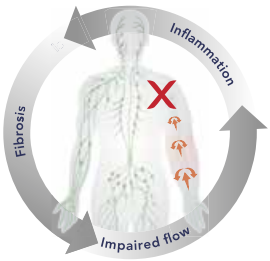
Program Discovery Process by the PureTech Team

- LYT-100 (deupirfenidone) was originally developed by Auspex Pharmaceuticals, Inc. (Auspex, now a wholly owned subsidiary of Teva Pharmaceuticals), a company that pioneered the deuteration technology and successfully developed deutetrabenazine (Austedo®), becoming the first and only deuterated drug that has received FDA approval[3]. We selected and acquired LYT-100 (from Teva Pharmaceuticals) in July 2019 based on insights into the lymphatic system gained internally and via unpublished findings through our network of collaborators, coupled with the relationships of our team members and their insights into the program while in development at Auspex. We believe that the commercial success of the first and only deuterated drug, Austedo, based on a comparable efficacy to tetrabenazine but a highly differentiated, favorable safety and tolerability profile, could potentially serve as a good precedence for LYT-100.

Patient Need & Market Potential

Fibrosis and Inflammation-Related Lung Diseases

LYT-100: Tackling Inflammatory & Fibrotic Diseases

LYT-100-ILD	LYT-100-COV	LYT-100-LYMPH
~130K in the US with **IPF**[11]	Over **500M** people have been infected by **COVID-19**[12]	**~1M** in the US with **lymphedema**[15]
	 *Fibrosis leads to chronic lung scarring and respiratory dysfunction, persisting post-discharge.	
• Progressive fibrotic diseases leading to fatal lung dysfunction. Current standards of care for IPF associated with significant tolerability issues • **Initiating registration-enabling studies in 1H 2022**	• Up to 1/3 of severe COVID-19 patients develop lung fibrosis[13] • Up to 54% of hospitalized COVID-19 patients develop lasting dyspnea[14] • **Topline results from Phase 2 expected in 1H 2022**	• Lymphatic damage initiates vicious cycle of inflammation & fibrosis which further impairs fluid flow & tissue regeneration[16,17] • **Topline results from Phase 2a POC expected in 2022**

- Fibrosis and inflammation are a common mechanism across several lung diseases. These are acute diseases with high mortality or that lead to long-term fibrosis; chronic diseases linked to a specific cause, like a virus or autoimmune disease; and diseases like IPF, where the causes are unclear but have been postulated to include viruses, genetic factors and a variety of environmental exposures. For the majority of these lung conditions, there are few approved treatments that address the underlying inflammation and fibrosis affecting the lungs. Many of these diseases are progressive, and there is a clear unmet need to halt the inflammation and progressive fibrosis in order to preserve lung function.

11 Martinez, F. J., Collard, H. R., Pardo, A., Raghu, G., Richeldi, L., Selman, M., Swigris, J. J., Taniguchi, H., Wells, A. U. (2017). Idiopathic pulmonary fibrosis. Nature Reviews Disease Primers, 3(17074). doi:https://doi.org/10.1038/nrdp.2017.74.

12 COVID-19 map. Johns Hopkins Coronavirus Resource Center. (2021). https://coronavirus.jhu.edu/map.html.

13 Han, X., Fan, Y., Alwalid, O., Li, N., Jia, X., Yuan, M., Li, Y., Cao, Y., Gu, J., Wu, H., & Shi, H. (2021). Six-month Follow-up Chest CT Findings after Severe COVID-19 Pneumonia. Radiology, 299(1), E177–E186. https://doi.org/10.1148/radiol.2021203153.

14 Lerum, T. V., Aaløkken, T. M., Brønstad, E., Aarli, B., Ikdahl, E., Lund, K., Durheim, M. T., Rodriguez, J. R., Meltzer, C., Tonby, K., Stavem, K., Skjønsberg, O. H., Ashraf, H., & Einvik, G. (2021). Dyspnoea, lung function and CT findings 3 months after hospital admission for COVID-19. The European respiratory journal, 57(4), 2003448. https://doi.org/10.1183/13993003.03448-2020.

15 Lymphedema. Vascular Cures. (2017). https://vascularcures.org/lymphedema/.

16 Gousopoulos, E., Proulx, S. T., Bachmann, S. B., Scholl, J., Dionyssiou, D., Demiri, E., Halin, C., Dieterich, L.C., Detmar, M. (2016). Regulatory T cell transfer ameliorates lymphedema and promotes lymphatic vessel function. JCI Insight, 1(16). doi:10.1172/jci.insight.89081.

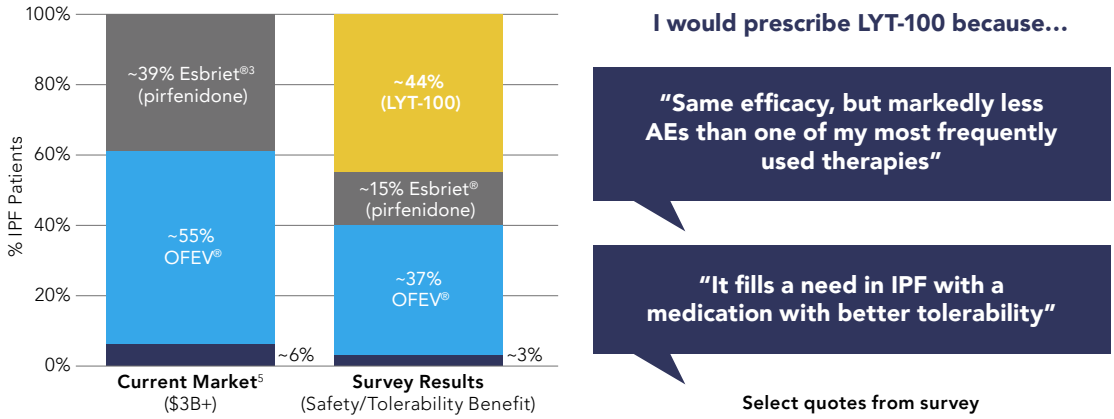
17 Avraham, T., Daluvoy, S., Zampell, J., Yan, A., Haviv, Y. S., Rockson, S. G., & Mehrara, B. J. (2010). Blockade of transforming growth factor-beta1 accelerates lymphatic regeneration during wound repair. The American journal of pathology, 177(6), 3202–3214. https://doi.org/10.2353/ajpath.2010.100594.

Patient Need & Market Potential (continued)

- IPF
  - There are approximately 130,000 people living with IPF in the U.S. IPF is a progressive condition characterized by irreversible scarring of the lungs that worsens over time, making it difficult to breathe. The prognosis of IPF is poor, with the median survival after diagnosis generally estimated at two to five years.
  - Even in IPF, for which pirfenidone is approved, there remains a need for more tolerable treatment options. Despite the limitations of this therapy, pirfenidone sales peaked above $1 billion each year from 2018 to 2021.

LYT-100-ILD: Independent Research Shows Profile Attractive to Surveyed Pulmonologists[18]

Pulmonologists would prescribe LYT-100 to ~44% of their new IPF patients (even without enhanced efficacy compared to SOC)



Certain results from this survey are depicted in the graphic above (right panel). Data from this survey are consistent with findings of independent publications that point to significant tolerability issues, particularly GI-based AEs, as the greatest limitations of the current standard of care in IPF.

- In the 2022 post-period, we engaged an independent third-party market research firm to conduct a survey of 100 pulmonologists who actively treat patients with IPF, to assess the potential commercial opportunity for LYT-100-ILD in IPF. In this survey, pulmonologists highlighted an unmet need for treatments with improved tolerability profiles. When physicians were asked the primary reasons patients discontinue or dose reduce current standard of care for IPF, 80-90% highlighted GI AEs as a main cause. Pulmonologists in this survey were also presented with a hypothetical profile[18] of LYT-100-ILD, labeled "Product X", that indicated an improved tolerability profile with comparable efficacy relative to standard of care in IPF. Based on this profile, physicians indicated they would prescribe Product X to nearly 44% of their new IPF patients. Furthermore, nearly 80% of physicians indicated they would prescribe Product X more than pirfenidone. Based on this survey, LYT-100 is expected to have a significant impact on the IPF market based on its improved tolerability profile and similar efficacy compared to standard of care, which is consistent with findings from the prior market research.
- Long COVID (PACS) Respiratory Complications and Related Sequelae
  - The COVID-19 pandemic has affected over 500 million people around the world. There is increasing data around the longer-term complications of COVID-19, referred to as Long COVID (PACS) including data regarding respiratory issues that persist following recovery. Survivors of the virus can have persistent shortness of breath and develop progressive lung fibrosis that could potentially last for years.
  - Post-acute injuries are hypothesized to be due to a cascade of inflammation and fibrosis that begins during the acute phase of COVID-19 and continues after the infection resolves. Up to one-third of severe COVID-19 patients develop lung fibrosis post symptom onset. Over 40% of hospitalized COVID-19 patients have lasting dyspnea and up to 33% of severe COVID-19 patients develop lung fibrosis.
  - COVID-19 post-acute injuries appear to mimic respiratory complications of other viral pneumonias like Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS). Up to one-third of SARS and MERS survivors had abnormal pulmonary testing and lung imaging findings that persisted for years.
- Lymphedema
  - Lymphedema is a chronic, disfiguring and painful condition that afflicts millions of people globally and is characterized by severe swelling in parts of the body, typically the arms or legs, due to the build-up of lymph fluid and inflammation, fibrosis and adipose deposition. By conservative estimates, lymphedema afflicts approximately one million people in the U.S., including approximately 500,000 breast cancer survivors. Secondary lymphedema is the most prevalent form of lymphedema. Secondary lymphedema can develop after surgery, infection, or trauma, and is frequently caused by cancer or cancer treatments such as radiation and chemotherapy, that cause damage to or mandate the removal of lymph nodes.
  - The current standard of care for lymphedema is symptom management, primarily with compression and physical therapy to control swelling. These approaches are cumbersome, uncomfortable and do not address the progression of the underlying disease. Even with management, many patients will progress from mild-to-moderate lymphedema to more severe forms. No approved drugs exist to treat the underlying causes of lymphedema. We believe the lack of treatments for lymphedema represents a major unmet medical need.

18 100 pulmonologists were surveyed, no pricing information/assumptions was shared. Research completed in the April 2022 post-period based on the latest target product profile and findings were consistent with our prior market research.

Milestones Achieved & Development Status

- In the January 2022 post-period, we announced results from a randomized, double-blind crossover study in healthy older adults demonstrating that approximately 50% fewer subjects treated with LYT-100 (deupirfenidone) experienced GI-related AEs compared to subjects treated with pirfenidone (17.4% vs. 34.0%).
  - The double-blind, randomized, crossover study evaluated the tolerability of LYT-100 550 mg TID versus pirfenidone 801 mg TID in 49 older healthy adults aged 60-79, an age group that is representative of the IPF patient population. The dose of LYT-100 used in this study was selected based on PK and modeling data from prior studies, which together suggest that 550 mg TID results in similar drug exposure levels achieved with 801 mg TID of pirfenidone. The study results demonstrated that 38% fewer subjects treated with LYT-100 experienced any AE compared with those treated with pirfenidone (30.4% vs. 48.9%). Additionally, approximately 50% fewer subjects experienced GI-related AEs with LYT-100 compared with pirfenidone (17.4% vs. 34.0%), most notably nausea (15.2% with LYT-100 vs. 29.8% with pirfenidone), which is the most common AE associated with pirfenidone. No serious AEs were reported in the study, and there was one AE-related discontinuation in each arm. Though not powered to show statistical significance, this study provides evidence that LYT-100 has the potential to offer an important tolerability advantage over pirfenidone and will help to inform our development plans with this therapeutic candidate in IPF.

LYT-100: Data to Date Demonstrate Tolerability Advantage Over Pirfenidone

LYT-100 demonstrates lower Cmax with same AUC compared to pirfenidone

Healthy Older Adult Crossover Study (N=49[19])		
TEAE	**LYT-100 550mg TID n (%)**	**Pirfenidone 801mg TID n (%)**
Gastrointestinal	**8 (17.4%)**	**16 (34.0%)**
– Nausea	7 (15.2%)	14 (29.8%)
– Vomiting	2 (4.3%)	3 (6.4%)
– Abdominal Pain/ Distension	1 (2.2%)	3 (6.4%)
Nervous System	**8 (17.4%)**	**15 (31.9%)**
– Headache	6 (13.0%)	9 (19.1%)
– Dizziness	1 (2.2%)	7 (14.9%)
– Somnolence	1 (2.2%)	2 (4.3%)

Clinical data demonstrate favorable tolerability

Multiple Ascending Dose Study[20]
Well-tolerated at all doses studied[21] without dose titration
All treatment-related **AEs** were **mild & transient**

Healthy Older Adult Crossover Study
Achieved **~50% reduction** in healthy older adults experiencing **GI-related AEs compared to pirfenidone**

TEAE = treatment emergent adverse event
Discontinuations for AEs: 1 during pirfenidone administration, 1 during LYT-100 administration

- In the January 2022 post-period, we announced Paul Ford, M.D., Ph.D., joined PureTech as SVP of Clinical Development to oversee the LYT-100 development program in IPF. Dr. Ford is an experienced clinical pulmonologist with more than 20 years of research and development expertise dedicated to IPF and other respiratory conditions. He has built and advanced programs from early-to late-stage development at companies including Novartis, Galapagos and Galecto, and he has been instrumental in the enrollment of nearly 1,500 patients with IPF across several clinical studies.
- In November 2020, we announced the completion of a Phase 1 randomized, double-blind multiple ascending dose (MAD) and food effect study, which was designed to evaluate the safety, tolerability and PK profile of LYT-100 in healthy volunteers. The study demonstrated favorable proof-of-concept for the tolerability and PK profile of LYT-100. In August 2021, we presented the results of the study at the virtual European Respiratory Society (ERS) International Congress. In November 2021, the full study was published in *Clinical Pharmacology in Drug Development*.
  - All AEs that were possibly or probably related to LYT-100 were mild and transient and there were no discontinuations. No serious AEs or dose-limiting toxicities were observed in the study. The maximum tolerated dose was not determined after dosing up to 1,000 mg twice per day.
  - The food effect portion of the study evaluated two common PK measures that are used to determine the optimal dose of a therapeutic candidate – area under the curve (AUC) and Cmax. Under fed conditions, the AUC of LYT-100 was reduced by about 19%, which is comparable to the AUC reduction of 16% seen with pirfenidone as stated in the Esbriet® U.S. Prescribing Information. The Cmax reduction observed with LYT-100 was 23%, while the Cmax reduction seen with pirfenidone was 49% as stated in the Esbriet® (pirfenidone) U.S. Prescribing Information.
- In 2021, we initiated additional Phase 1 clinical trials to further evaluate the PK, dosing and tolerability of LYT-100 in healthy volunteers and healthy older adults to inform the clinical development of LYT-100 across multiple indications. Results from these studies demonstrated that LYT-100 was well-tolerated at 824mg TID dosing with low rates of GI AEs that were comparable to placebo. These results will further inform our dose-ranging study design in treatment-naïve IPF patients.
- In April 2021, we announced the formation of a Clinical Advisory Board for IPF and other PF-ILDs. These physicians and researchers with deep expertise in the clinical development of novel therapies in PF-ILDs include Bill Bradford, M.D., Ph.D., biopharma advisor with broad expertise in drug development; Vincent Cottin, M.D., Professor of Respiratory Medicine at Université Claude Bernard Lyon and Coordinator of the National Coordinating Reference Center for Rare Pulmonary Diseases at Louis Pradel Hospital, Hospices Civils de Lyon, Lyon, France; Kevin Flaherty, M.D., Professor at the University of Michigan specializing in IPF and other ILDs; Toby Maher, M.D., Ph.D., Professor of Clinical Medicine and Director of Interstitial Lung Disease at Keck School of Medicine of the University of Southern California; Paul Noble, M.D., Chair of the Department of Medicine at Cedars-Sinai Medical Center and a noted researcher in lung inflammation and fibrosis; and Marlies Wijsenbeek, M.D., Ph.D., pulmonary physician at the Erasmus Medical Center.
- Long COVID (PACS) respiratory complications and related sequelae
  - In December 2020, we announced the initiation of a global, randomized, double-blind, placebo-controlled Phase 2 trial to evaluate the efficacy, safety and tolerability of LYT-100-COV in adults with Long COVID respiratory complications and related sequelae.
  - In 2021, we initiated the open-label extension of the LYT-100-COV Phase 2 trial in patients who completed the first portion of the trial. The primary endpoint of the extension trial will measure change in distance walked on the 6MWT, with secondary endpoints to assess the longer-term safety and tolerability of LYT-100 up to 182 days of treatment.
  - In preclinical rodent studies, LYT-100 was observed to suppress levels of IL-6 and TNF-alpha induced by lipopolysaccharide administration, which we believe reinforces the potential of LYT-100 to reduce the acute inflammation and cytokine release that has been associated with SARS-CoV-2 infection. Anti-fibrotic activity was also observed with LYT-100 in preclinical studies. Lung fibrosis has also been observed in some patients following the acute phase of COVID-19. For more information on our clinical trial, visit ClinicalTrials.gov.

19 44 completed study (5 early terminated: 2 for AEs, 3 for non-medical reasons).
20 Chen, M.C., Korth, C.C., Harnett, M.D., Elenko, E. and Lickliter, J.D. (2022), A Randomized Phase 1 Evaluation of Deupirfenidone, a Novel Deuterium-Containing Drug Candidate for Interstitial Lung Disease and Other Inflammatory and Fibrotic Diseases. Clinical Pharmacology in Drug Development. https://doi.org/10.1002/cpdd.1040.
21 LYT-100 was administered in doses of 100 mg, 250 mg, 500 mg, 750 mg and 1000 mg BID over five days.

Milestones Achieved & Development Status (continued)	• Lymphedema – In December 2020, we announced the initiation of a Phase 2a proof-of-concept study of LYT-100-LYMPH in patients with breast cancer-related, upper limb secondary lymphedema. The primary endpoint of the study is safety and tolerability of LYT-100-LYMPH. Secondary endpoints include outcome measures relevant to lymphedema, including relative limb volume, bioimpedance spectroscopy (a measure of extracellular fluid change), tonometry (a measure of fibrosis) and serum levels of inflammatory and fibrotic biomarkers. The study will also examine patient reported outcomes using validated self-report instruments specific to upper-arm lymphedema. The study is not adequately powered to evaluate drug effect versus placebo with statistical significance, but we believe the totality of the data will be suitable to inform the design of future clinical protocols. For more information on our clinical trial, visit ClinicalTrials.gov. – In preclinical studies, LYT-100 showed greater anti-fibrotic and anti-inflammatory activity compared to pirfenidone. Additionally, LYT-100 was tested by one of our academic collaborators in a preclinical model of lymphedema which showed that LYT-100 halted progression of lymphedema and reduced the overall volume of the affected area. These results still need to be confirmed in clinical trials.
Expected Milestones	• We plan to initiate a Phase 2 dose-ranging trial of LYT-100 in patients with IPF in the first half of 2022 with topline results expected by the end of 2023. We also plan to pursue a streamlined development program for LYT-100 in IPF, capitalizing on efficiencies of the 505(b)(2) pathway. Pending positive clinical and regulatory feedback, the program will advance into a Phase 3 study. We believe the results of the Phase 2 study, together with a Phase 3 study, could serve as the basis for registration in the U.S. • Topline results from the Phase 2 trial of LYT-100-COV in adults with Long COVID respiratory complications and related sequelae are anticipated in the first half of 2022. • We expect topline results from the Phase 2a proof-of-concept study of LYT-100-LYMPH in patients with breast cancer-related, upper limb secondary lymphedema in 2022.
Intellectual Property	• As of December 31, 2021, the LYT-100 patent portfolio includes 31 active patents acquired, and one issued patent and one patent application licensed from Auspex. These patents and application provide broad coverage of compositions of matter, formulations and methods of use for deuterated pirfenidone, including the LYT-100 deupirfenidone compound, comprising six issued U.S. patents which are expected to expire in 2028 (without patent term extensions, which could extend the exclusivity to 2033), one U.S. patent which is expected to expire in 2035 and 25 patents issued in 23 foreign jurisdictions, without taking into account any possible patent term extension or regulatory exclusivities. We have also filed additional patent applications on deupirfenidone, including 13 pending U.S. patent applications, three international PCT applications and 13 foreign applications directed to the use of deuterated pirfenidone, including LYT-100, for the treatment of a range of conditions involving inflammation and fibrosis, including lung disease (IPF and Long COVID respiratory complications and related sequelae) and disorders of lymphatic flow, such as lymphedema. We expect that any issued patents claiming priority to these applications will expire in 2039 through 2042, exclusive of possible patent term adjustments or extensions or other exclusivities.

LYT-100 Program

Therapeutic Candidate[1]	Indication	Discovery	Preclinical	Phase 1	Phase 2	Phase 3
LYT-100-ILD Deupirfenidone	IPF					
LYT-100-COV Deupirfenidone	Long COVID[2] respiratory complications and related sequelae					
LYT-100-LYMPH Deupirfenidone	Lymphatic flow disorders, including lymphedema					

Phase completed Phase in progress Registration-enabling studies to begin in 1H2022

LYT-200

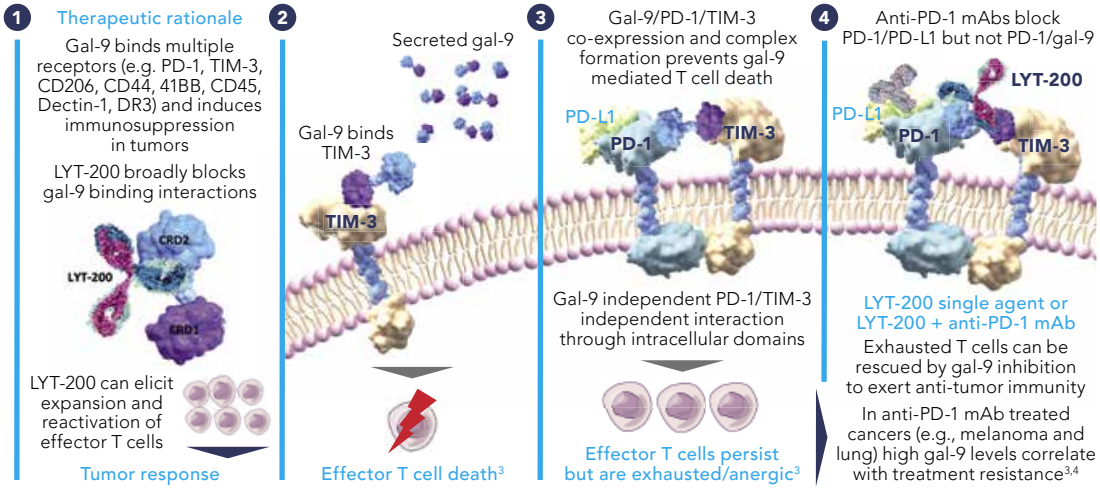
Therapeutic Candidate[1]	PureTech Ownership	Indication	Stage of Development
LYT-200	Wholly-owned	Solid tumors	Phase 1

- LYT-200 is a fully human IgG4 monoclonal antibody, or mAb, designed to inhibit the activity of galectin-9, a key molecule expressed by tumors and immune cells and shown to suppress the immune system from recognizing and destroying cancer cells. We are developing LYT-200 for difficult-to-treat cancer indications, including pancreatic ductal adenocarcinoma (PDAC), colorectal cancer (CRC) and cholangiocarcinoma (CCA).

Key Points of Innovation & Differentiation

- Immune checkpoint inhibitors, including therapies that target programmed cell death protein 1, or PD-1, programmed death ligand 1, or PDL-1, and cytotoxic T-lymphocyte-associated antigen 4, or CTLA-4, have been developed to counteract multiple mechanisms of immune evasion by a number of different tumor types. Recent reports suggest that marketed drugs against these targets had sales exceeding $28 billion in 2020[2]. Unfortunately, a large proportion of patients, especially those with immunologically silent tumors such as PDAC, CCA and some types of CRC respond sub-optimally to such agents.
- Galectin-9 promotes and facilitates multiple immunosuppressive pathways by, for example, expanding regulatory T cells, shifting macrophages from the M1 to M2 phenotype, and inducing apoptosis of activated CD4+ and CD8+ T cells. High expression of galectin-9 is evident in tumors and in cancer patients' blood and correlates with poor survival outcomes and aggressive disease in multiple solid tumor types. We are advancing LYT-200 to inhibit the multiple effects of galectin-9 and thereby potentially removing a key immunosuppressive barrier that would enable the immune system to attack and destroy the tumor.

Galectin-9 is a ligand for PD-1 regulating T cell death and immune responses in PD-1/PDL-1 expressing tumors



- A 2021 study published in *Nature Communications* proposed that the molecular mechanism by which PD-1 and galectin-9 interact to shield tumors from the immune system demonstrates for the first time that galectin-9 is a ligand for PD-1 and emphasizes its importance as a promising target for immunotherapy[3]. The work revealed that PD-1 physically interacts with galectin-9 and TIM-3 to attenuate galectin-9/TIM-3-induced T cell apoptosis and maintain effector T cells in the tumor microenvironment in an exhausted functional state. It also showed that interferons significantly upregulate galectin-9 expression and secretion in both immune and cancer cells. Overall, the work provided further evidence that galectin-9 acts as a key regulator of the immune response to tumors and supports its importance as a potential target for cancer treatment.
- Under normal physiological conditions, galectin-9 is expressed at low levels, which supports the potential safety of LYT-200 in clinical settings. Lack of toxicity/tolerability issues to date in our good laboratory practice (GLP) studies with LYT-200 – even at extremely high doses, such as 300 mg/kg in non-human primates (~100 mg/kg human equivalent dose) – further supports this view.
- We are not aware of any other clinical development program targeting galectin-9 as a therapeutic target, and thus, we believe that LYT-200 may represent the most advanced clinical program against this target. None of the other human galectins have been documented to play such a global role as galectin-9 in immunosuppression in the context of cancer. We also believe that LYT-200 has the potential to be used as a single agent and safely in combination with checkpoint inhibitors and other chemotherapeutics, depending on the cancer.

Program Discovery Process by the PureTech Team

- In order to identify approaches with the potential to provide significant therapeutic benefit to cancer patients, we undertook a global, proactive search to identify therapeutic targets that mediate multiple mechanisms of immunosuppression. Through our extensive network of advisors and collaborators, we identified a foundational immunosuppressive mechanism involving galectin-9, the therapeutic target of LYT-200, which was the basis of certain intellectual property that we licensed from New York University prior to publication in *Nature Medicine*[5].

Patient Need & Market Potential

- In the U.S., there are approximately 62,210 new pancreatic cancer patients, of which 52% present with metastatic disease, approximately 151,030 new CRC patients, of which 22% present with metastatic disease, and approximately 8,000 new CCA patients, of which 50% present with metastatic disease, in each case, per year. Unfortunately, a large proportion of patients, especially those with immunologically silent tumors such as PDAC, CCA and some types of CRC respond sub-optimally to immune checkpoint inhibitors, representing a significant patient population that has yet to receive benefit from any immuno-therapy agents.

Milestones Achieved & Development Status

- In November 2021, the FDA granted orphan drug designation to LYT-200 for the treatment of pancreatic cancer. The FDA grants orphan drug designation to novel drug and biologic products for the treatment, diagnosis or prevention of conditions affecting fewer than 200,000 persons in the U.S. Orphan drug designation qualifies PureTech for incentives under the Orphan Drug Act, including tax credits for some clinical trials and eligibility for seven years of market exclusivity in the U.S. if the drug is approved, in addition to our broad intellectual property coverage which can extend the exclusivity into 2038.

1 We have an active IND on file with the FDA for LYT-200. The FDA and corresponding regulatory authorities will ultimately review our clinical results and determine whether our wholly-owned therapeutic candidates are safe and effective. No regulatory agency has made any such determination that LYT-200 is safe or effective for use by the general public for any indication.

2 GlobalData Sales and Forecast Database (2021).

3 Yang, Riyao, et al. "Galectin-9 Interacts with PD-1 and TIM-3 to Regulate T Cell Death and Is a Target for Cancer Immunotherapy." Nature Communications, 5 Feb. 2021, www.nature.com/articles/s41467-021-21099-2 (preclinical data).

4 Limagne, E., Richard, C., Thibaudin, M., Fumet, J. D., Truntzer, C., Lagrange, A., Favier, L., Coudert, B., & Ghiringhelli, F. (2019). Tim-3/galectin-9 pathway and mMDSC control primary and secondary resistances to PD-1 blockade in lung cancer patients. Oncoimmunology, 8(4), e1564505. https://doi.org/10.1080/2162402X.2018.1564505. (preclinical data).

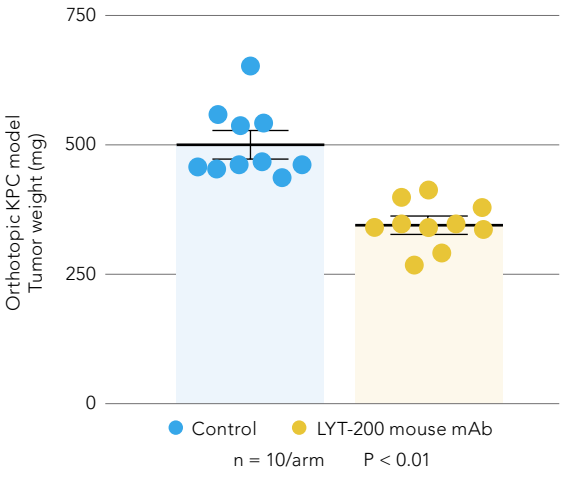
5 Daley, D., Mani, V., Mohan, N. et al. Dectin 1 activation on macrophages by galectin 9 promotes pancreatic carcinoma and peritumoral immune tolerance. Nat Med 23, 556 – 567 (2017). https://doi.org/10.1038/nm.4314.

Milestones Achieved & Development Status (continued)

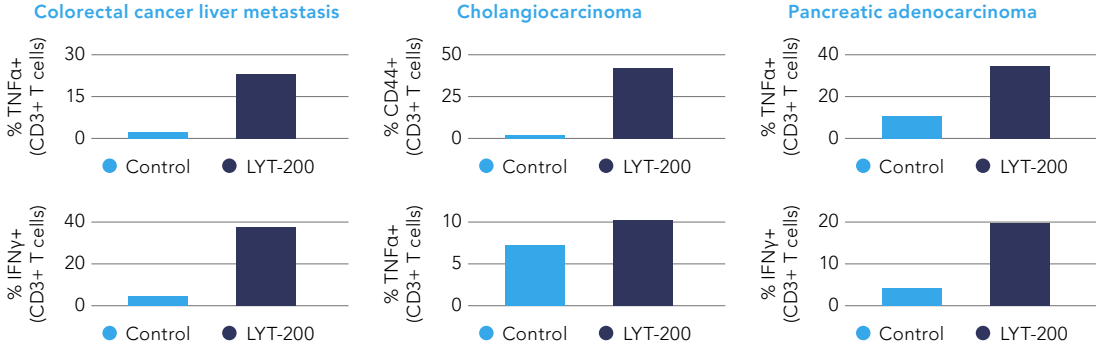
– In November 2021, we announced that a poster presentation describing the adaptive Phase 1/2 trial of LYT-200 for the potential treatment of difficult-to-treat solid tumors was given at the Society for Immunotherapy of Cancer (SITC) 36th Annual Meeting.
– In July 2021, we announced a clinical trial and supply agreement with an affiliate of BeiGene, Ltd. to evaluate BeiGene's tislelizumab, an anti-PD-1 monoclonal antibody, in combination with LYT-200. Under the terms of the agreement, we will maintain control of the LYT-200 program, including global R&D and commercial rights. BeiGene has agreed to supply tislelizumab for use in combination with LYT-200 for the planned Phase 2 study cohorts.
– In 2021, we progressed our adaptive Phase 1/2 clinical trial to evaluate LYT-200 as a potential treatment for metastatic solid tumors. The primary objective of the Phase 1 portion of the trial is to assess the safety and tolerability of escalating doses of LYT-200 in order to identify a dose to carry forward into the Phase 2 portion of the trial. The Phase 1 trial will also assess LYT-200's PK and PD profiles. Pending these results, we intend to initiate the Phase 2 expansion cohort portion of the trial, which is designed to evaluate LYT-200 either alone and/or in combination with BeiGene's tislelizumab or chemotherapy and anti-PD-1 therapy for the treatment of multiple solid tumor types, including pancreatic cancer and CCA. For more information on our clinical trial, visit ClinicalTrials.gov.

• Preclinical results
– LYT-200 has been observed to have high specificity for its primary target galectin-9: This was established using a protein array that assessed binding of LYT-200 to more than 5,000 cell bound and secreted human proteins.
– LYT-200 blocks the galectin-9-CD206 interaction: LYT-200 is able to block functional activity of galectin-9, including its interactions with a specific binding partner/receptor, e.g., CD206. This was established using an ELISA assay demonstrating a galectin-9/CD206 interaction, which could be inhibited by the addition of LYT-200.
– LYT-200 protects MOLM-13 T cells from galectin-9-mediated apoptosis: LYT-200 has also been observed to protect T cells from apoptosis mediated by galectin-9. For example, galectin-9 was shown to significantly increase apoptotic death of MOLM-13 cells. Treatment with LYT-200 in the presence of galectin-9 significantly reduced the percentage of T cells undergoing apoptosis in a dose dependent manner.
– LYT-200 exceeded anti-PD-1 activity in the B16F10 melanoma model, a gold standard for measuring checkpoint inhibitor efficacy: To further characterize the potential of LYT-200 as a single agent, we created a mouse isotype of LYT-200 (mIgG1-200). mIgG1 200 (LYT-200 designed for mouse in vivo models) reduced mean tumor weights by approximately 50% while an anti-PD-1 antibody reduced mean tumor weights by approximately 22%, which is what is typically seen in the model. We also observed that when an anti-PD-1 antibody was used in combination with mIgG1-200, the number of tumor-infiltrating cytotoxic T cells detected in tumors approximately doubled. These data demonstrate efficacy of mIgG1-200, both as a single agent and in combination with a checkpoint inhibitor.
– LYT-200 inhibited tumor growth, induced T cell activation and increased survival in the orthotopic pancreatic cancer KPC model where anti-PD1 agents are ineffective: The orthotopic KPC mouse model is commonly used as a preclinical model for evaluating PDAC biology and therapeutic agent efficacy. Anti-PD-1 checkpoint inhibitors have previously proven ineffective in this syngeneic model. Single agent activity of mIgG1-200 was observed in the KPC mouse pancreatic cancer model as illustrated in the figure below. We have evaluated the combination of mIgG1 200 with the standard of care for pancreatic cancer, (e.g., chemotherapy: gemcitabine/nab-paclitaxel). We observed a clear survival improvement with mIgG1 200, both as a single agent and in combination with clinical standard of care chemotherapy.
– LYT-200 activates T cells in cultured patient-derived organoid tumors, or PDOTs: One of the major challenges in oncology research is the translation from mouse models to humans, particularly in the case of immuno-oncology. To address this concern, we explored LYT-200 activity in cultured PDOTs that mimic human tumor composition within the context of a tumor microenvironment. The aim of treating PDOTs was to assess the ability of LYT-200 to induce T cell activation, which may predict how LYT-200 would behave in humans. LYT-200 potently and reproducibly activated T cells in 56% of the samples tested (n=23).

LYT-200 mouse mAb activity in orthotopic pancreatic cancer KPC model



Examples of in vitro T cell activation with LYT-200[6]



– GLP toxicology studies were carried out in Sprague Dawley rats and cynomolgus monkeys. No safety pharmacology findings that were attributed to LYT-200 at doses as high as 300 mg/kg/week were observed with repeat dose exposure.

6 Analyzed n = 23 tumor samples; Success defined as: >20% upregulation of at last two out of three T cell activation markers; Success achieved in 56% of tumors with majority showing >2 fold activation; Representative data from individual tumors per annotated tumor type are shown.

Expected milestones	• LYT-200 is currently being evaluated as a single agent in the first stage of an adaptive Phase 1/2 clinical trial. Pending these results, we intend to initiate the Phase 2 expansion cohort portion of the trial, which is designed to evaluate LYT-200 both as a single agent and in combination with chemotherapy or BeiGene's tislelizumab, an anti-PD-1 mAb. We expect to report topline results from the Phase 1 portion in the first half of 2022.
Intellectual property	• We have broad intellectual property coverage for these antibody-based immunotherapy technologies, including exclusive rights to six families of patent filings that are exclusively licensed from or co-owned with New York University which cover antibodies that target galectin-9, including LYT-200, methods of using these antibodies and related immuno-oncology technologies. In addition, the intellectual property portfolio includes three families of PureTech-owned patent applications covering the use of anti-galectin-9 antibodies in the diagnosis and treatment of solid tumors. • As of December 31, 2021, there are nine families of intellectual property within this patent portfolio covering compositions of matter for antibodies targeting galectin-9, including LYT-200, and methods of use for the treatment of solid tumors, such as pancreatic cancer, CRC, melanoma, gastric cancer, breast cancer and various other cancers. This intellectual property comprises two issued U.S. patents which are expected to expire in 2038, 10 pending U.S. patent applications, which if issued, are expected to expire 2037-2042 (exclusive of possible patent term adjustments or extensions or other exclusivities), four international PCT applications, twenty-four pending foreign applications and five issued patents in foreign jurisdictions.

LYT-200 Program

Therapeutic Candidate[1]	Indication	Discovery	Preclinical	Phase 1	Phase 2	Phase 3
LYT-200 Anti-Galectin-9 mAb	Solid tumors					

Phase completed Phase in progress

LYT-210

Therapeutic Candidate[1]	PureTech Ownership	Indication	Stage of Development
LYT-210	Wholly-owned	Solid tumors	Preclinical

- LYT-210 is a preclinical therapeutic candidate designed to target immunomodulatory gamma delta-1 T cells, and is being developed for a range of cancer indications.

Key Points of Innovation & Differentiation

- Immune checkpoint inhibitors, including therapies that target PD-1, PDL-1 and cytotoxic T-lymphocyte-associated antigen 4, or CTLA-4, have been developed to counteract multiple mechanisms of immune evasion by a number of different tumor types. Recent reports suggest that marketed drugs against these targets had sales exceeding $28 billion in 2020[2]. Unfortunately, a large proportion of patients, especially those with immunologically silent tumors such as PDAC, CCA and some types of CRC, respond sub-optimally to such agents.

Monoclonal antibody aimed at immunosuppressive gamma delta-1 T cells

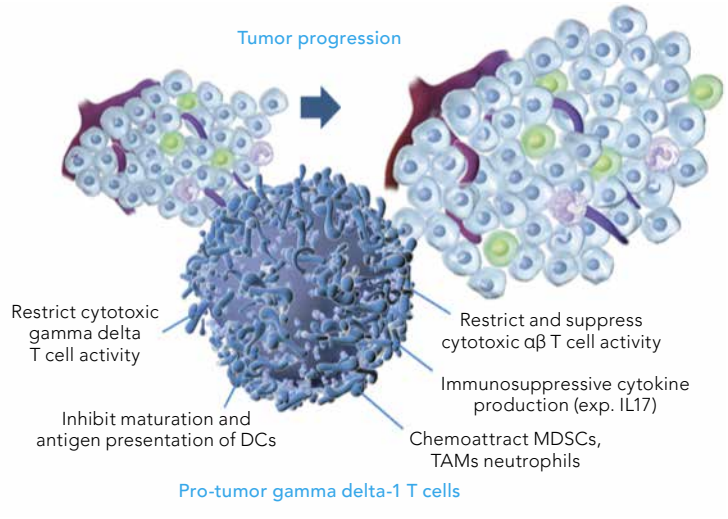
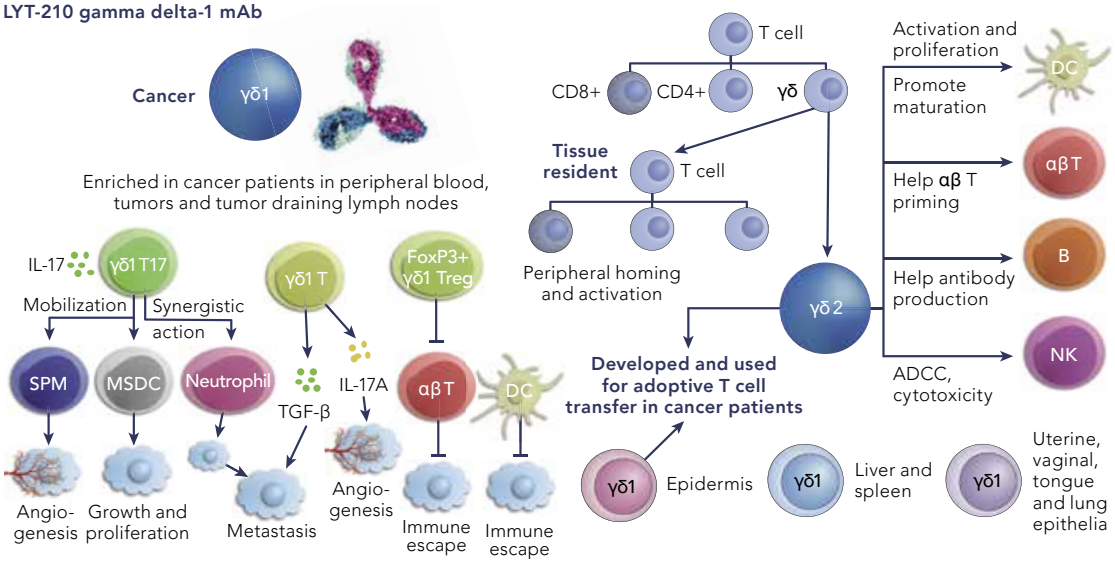


Image adapted from CellPress: REVIEW: gamma delta T cells: Unexpected Regulators of Cancer Development and Progression.

Key
DC = dendritic cell
TAM = tumor associated macrophage
MDSC = myeloid derived suppressor cell
IL17 = interleukin 17
αβ = alpha beta
γδ = gamma delta
γδ1 = gamma delta-1
γδ1 T17 = gamma delta interleukin 17 producing cells
γδ1 Treg = gamma delta-1 T regulatory cell
γδ2 = gamma delta-2
FoxP3 = forkhead box P3
SPM = small peritoneal macrophages
MSDC = myeloid derived suppressor cells
TGF-β = transforming growth factor beta
B = B cells
NK = natural killer cells
CD8+ = cluster of differentiation 8
CD4+ = cluster of differentiation 4

LYT-210 gamma delta-1 mAb



- Gamma delta-1 T cells execute potent immunosuppressive function via multiple mechanisms, as illustrated on the left side of the figure above (LYT-210 gamma delta-1 mAb), which facilitates cancer progression. We have designed LYT-210 to eliminate gamma delta-1 T cells, and thereby potentially relieve immunosuppression, which we believe could enable immune mediated cancer attack.
- We believe that gamma delta-1 T cells represent an important new IO target because they:
  - Activate multiple immunosuppressive pathways in the tumor microenvironment, or TME;
  - Have expression correlated with poor outcomes for multiple solid tumor types; and
  - Target immunosuppressive gamma delta T cells in vivo, which improved survival and reactivated cytotoxic T cells in the TME in the KPC orthotopic pancreatic cancer mouse model where approved checkpoint inhibitors are ineffective.
- We are targeting immunosuppressive, tumorigenic gamma delta-1 T cells for depletion, rather than administering cytotoxic gamma delta-2 T cells as a cell therapy, which is a complementary gamma delta T cell modality.

Program Discovery Process by the PureTech Team

- In order to identify approaches with the potential to provide significant therapeutic benefit to cancer patients, we undertook a global, proactive search to discover important new scientific insights and technologies that could address the challenge of multiple mechanisms of immunosuppression in current therapeutics. As a result of this search, and through our extensive network of advisors and collaborators, we identified a foundational immunosuppressive mechanism involving immunosuppressive gamma delta-1 T cells, which was the basis of LYT-210.

1 The FDA and corresponding regulatory authorities will ultimately review our clinical results and determine whether our wholly-owned therapeutic candidates are safe and effective. No regulatory agency has made any such determination that LYT-210 is safe or effective for use by the general public for any indication.
2 GlobalData Sales and Forecast Database, 2020 sales data pulled 1/24/2022.

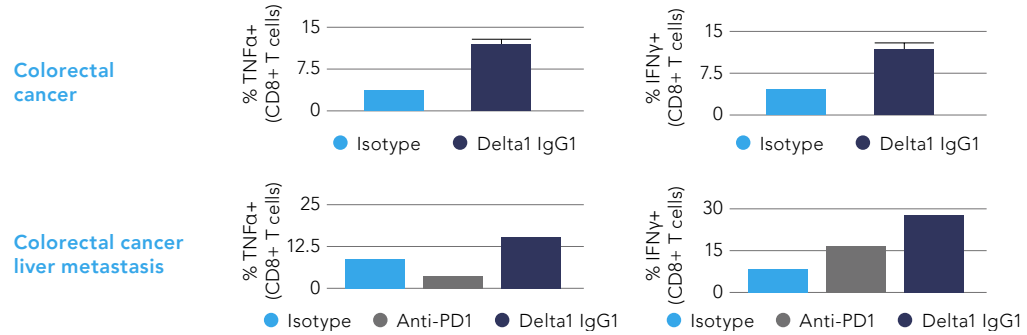
Patient Need & Market Potential

- In the U.S., there are approximately 62,210 new pancreatic cancer patients, of which 52% present with metastatic disease, approximately 151,030 new CRC patients, of which 22% present with metastatic disease, and approximately 8,000 new CCA patients, of which 50% present with metastatic disease, in each case, per year. Unfortunately, a large proportion of patients, especially those with immunologically silent tumors such as PDAC, CCA and some types of CRC respond sub-optimally to immune checkpoint inhibitors, representing a significant patient population that has yet to receive benefit from any immuno-therapy agents.

Milestones Achieved & Development Status

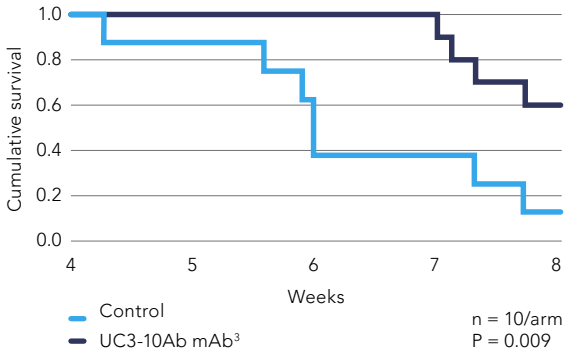
- In April 2021, we presented new research at the American Association for Cancer Research (AACR) Annual Meeting demonstrating that LYT-210 is both highly specific and highly potent, rapidly inducing cell death of immunomodulatory gamma delta-1 T cells, while sparing other T cells, such as cytotoxic gamma delta T cells, that play important roles in a healthy immune response. The research was conducted using both patient blood and cancer tissue.
- Antibodies against gamma delta-1 T cells reactivated immunosuppressed T cells in the TME in PDOTs: To better assess the potential activity of the anti-delta-1 antibody, we employed PDOTs from primary and metastatic tumors spanning various solid tumor types such as pancreatic, CRC, CCA, hepatocellular cancer and neuroendocrine tumors of the gastrointestinal (GI) tract in order to assess the prevalence of tumor-infiltrating gamma delta-1 T cells and the capacity of the antibodies to restore tumor-infiltrating immune cell effector activity. We observed positive responses in approximately 60% of the PDOTs we analyzed, representing 19 patients, which showed that direct treatment of PDOTs with LYT-210 resulted in robust reactivation of effector T cells.
- The figure below illustrates representative data from CRC patients, from a collection of 19 human tumor organoid samples where we ran this experiment.

Examples of *in vitro* T cell activation with antibodies against gamma delta-1 T cells



- Absence of gamma delta T cells greatly increased survival in a pancreatic cancer mouse model: In order to assess the relevance of gamma delta T cells in the development and progression of pancreatic cancer, we assessed the survival of immunocompetent mice which have gamma delta T cells (wild type) in a KPC mouse pancreatic model. Mice were treated with an antibody, UC3-10A6, which functionally blocks immunosuppressive mouse gamma delta T cells. As shown in the figure below, when mice harboring pancreatic tumors are treated with an antibody against immunosuppressive gamma delta T cells, survival was greatly increased, as represented by the navy curve.
- Mucosa-infiltrating pathogenic gamma delta-1 T cells may contribute to autoimmune diseases: Intraepithelial lymphocytes expressing gamma delta-1 T cells are tissue-resident T cells that play a key role in homeostasis of the intestinal epithelium. It has been recently observed that chronic inflammation can permanently reconfigure the tissue-resident T cell compartment resulting in the repopulation of the GI mucosa with pathogenic and cytotoxic gamma delta-1 T cells. Establishment of pathogenic gamma delta-1 T cells along the GI tract tilts the gut environment towards a chronic inflammatory state, contributing to the pathophysiology of GI tract and inflammatory diseases, such as refractory celiac disease.

Pancreatic cancer mouse survival with gamma delta T cell depletion and blockage



Expected Milestones

- We expect to complete additional biomarker studies for LYT-210 in 2022.

Intellectual property

- We have broad intellectual property coverage for these antibody-based immunotherapy technologies, including exclusive rights to two patent families that are exclusively licensed from or co-owned with New York University which cover antibodies that target immunosuppressive agents and mechanisms and methods of use for use related immuno-oncology technologies and antibodies directed to pro-inflammatory gamma delta T cells for use in the treatment of inflammatory conditions, such as autoimmune disorders.
- As of December 31, 2021, there are two families covering compositions of matter and methods of use for antibodies targeting gamma delta-1 T cells, including LYT-210, which are directed to the use of these antibodies for the treatment of cancer. This intellectual property in total comprises one granted U.S. patent, two pending U.S. patent applications and eight foreign patent applications. Any patents issuing from pending applications with respect to LYT-210 are expected to expire in between 2037 and 2041, of which expiration dates are exclusive of possible patent term adjustments or extensions or other periods of exclusivity.

LYT-210 Program

Therapeutic Candidate[1]	Indication	Discovery	Preclinical	Phase 1	Phase 2	Phase 3
LYT-210 Anti-Delta-1 mAb	Solid tumors					

Phase completed Phase in progress

3 Tool antibody that blocks mouse immunosuppressive gamma delta T cells.

LYT-300

Therapeutic Candidate[1]	PureTech Ownership	Indication	Stage of Development
LYT-300	Wholly-owned	Neurological and neuropsychological conditions	Phase 1

- Using our Glyph platform, which harnesses the natural trafficking of dietary lipids via the lymphatics, we have developed LYT-300, an oral lipid prodrug version of allopregnanolone. By trafficking LYT-300 via the lymphatics, we are able to overcome first-pass metabolism by the liver and achieve significant oral bioavailability of natural allopregnanolone in preclinical models. In 2021, we initiated a Phase 1 clinical study of LYT-300 in healthy volunteers as part of our ongoing strategy for developing this agent as a potential treatment for neurological and neuropsychological conditions with significant unmet need, such as depression, anxiety, sleep disorders, fragile X tremor-associated syndrome, essential tremor and epileptic disorders, among others.

Key Points of Innovation & Differentiation

- Allopregnanolone, a positive allosteric modulator of $GABA_A$ receptors, has therapeutic potential across a wide range of neurological conditions like depression, epilepsy and other neurological and neuropsychological conditions, but has poor oral bioavailability as a result of first-pass liver metabolism.
- An intravenous formulation of allopregnanolone is approved by the FDA as a 60-hour infusion for the treatment of post-partum depression, though the method of administration has limitations.
- To overcome the poor oral bioavailability of allopregnanolone, medicinal chemistry approaches have been applied to synthesize orally bioavailable analogs. Several of these modified allopregnanolone analogs have demonstrated varying degrees of clinical activity across different indications. The variable clinical activity of these compounds may be due to the possibility that chemical modifications are interfering with optimal $GABA_A$ receptor engagement and consequently their on-target mode of action. Hence, these chemically distinct analogs of allopregnanolone may not have the same pharmacologic effects as the natural unmodified allopregnanolone.
- Using our proprietary Glyph technology, which is designed for lymphatic targeting and to avoid first-pass metabolism, we have developed LYT-300, an oral prodrug of the endogenous, natural neurosteroid, allopregnanolone.
- Results from preclinical studies conducted thus far have demonstrated that LYT-300 is orally bioavailable and that relevant concentrations may be achievable in human plasma. One example of the data we have generated in non-human primates is shown below.

Program Discovery Process by the PureTech Team

- LYT-300 is the most advanced therapeutic candidate developed from our synthetic lymphatic-targeting chemistry platform called Glyph, which employs the body's natural lipid absorption and transport process to orally administer drugs via the lymphatic system.

Patient Need & Market Potential

- Allopregnanolone and related endogenous neurosteroids have been recognized for their potential to treat a range of neurological and neuropsychological conditions including depression, anxiety, sleep disorders, fragile X tremor-associated syndrome, essential tremor and epileptic disorders, among others. The major hurdles associated with the translation of these compounds have been:
  - The inability to create oral formulations of these neurosteroids; and
  - The inability to chronically administer compounds to patients
- An injectable formulation of allopregnanolone, which was approved by the FDA as a 60-hour infusion to treat postpartum depression, speaks to the challenges that limit the scope of clinical translation with this class of compounds.
- Oral formulations of allopregnanolone and other neurosteroids could potentially have significant advantages for the potential treatment of a range of neurological and neuropsychological conditions.

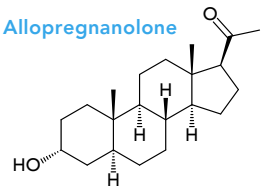
LYT-300: Oral Allopregnanolone for Neurological and Neuropsychological Conditions

The graph below depicts the dose-normalized plasma levels of free allopregnanolone after a single oral drug administration (equivalent to 2.8 mg/kg allopregnanolone) to non-human primates that were fed a standardized diet prior to dosing:

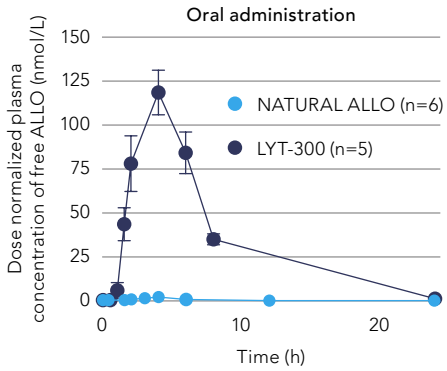
Brexanalone for IV injection
marketed as Zulresso®[2]

Required 60-hr IV infusion limits usage

Allopregnanolone



LYT-300 Systemic Exposure
Non-Human Primate



LYT-300 Development Rationale

- Designed to avoid first-pass metabolism by trafficking via the lymphatic system
- Oral bioavailability observed in canine and non-human primate PK studies
- Results from Phase 1 clinical study expected in 2H 2022

Oral administration

1 The FDA and corresponding regulatory authorities will ultimately review our clinical results and determine whether our wholly-owned therapeutic candidates are safe and effective. No regulatory agency has made any such determination that LYT-300 is safe or effective for use by the general public for any indication.

2 Zulresso® is a trademark of Sage Therapeutics and is not owned by or affiliated with PureTech Health. LYT-300 is an investigational drug not approved by any regulatory authority.

Milestones Achieved & Development Status	• In December 2021, we initiated a Phase 1 clinical study of LYT-300 in healthy volunteers as part of our ongoing strategy to develop this agent as potential treatment for neurological and neuropsychological conditions, including depression, anxiety, sleep disorders, fragile X tremor-associated syndrome, essential tremor and epileptic disorders, among others. The Phase 1 study of LYT-300 involves multiple parts, including the evaluation of a single ascending dose, multiple ascending doses and the effect of food on oral absorption of the prodrug. Safety, tolerability and PK will be assessed. Given the $GABA_A$ receptor modulating activity of allopregnanolone, the study will also explore the impact of LYT-300 on beta-EEG, a marker of $GABA_A$ target engagement, thus potentially providing early insights into the mechanistic effects of LYT-300. • In December 2021, we presented preclinical proof-of-concept data at the 60th American College of Neuropsychopharmacology (ACNP) Annual Meeting that support the clinical advancement of LYT-300 for the potential treatment of neurological and neuropsychological conditions. The data presented at ACNP showed that systemic exposure of natural allopregnanolone was achieved after oral administration of LYT-300 in multiple preclinical models of increasing complexity. In contrast, systemic levels of allopregnanolone were not observed following oral administration of natural unmodified allopregnanolone. These results demonstrate the potential of the Glyph technology platform to enhance the systemic absorption of natural bioactive molecules and other small molecules with poor oral bioavailability. • Oral bioavailability of LYT-300 has been confirmed in small and large animal PK studies. Results support the potential utility of this prodrug approach for oral administration of natural allopregnanolone and other small molecule therapeutics with intrinsic liabilities related to hepatic first-pass metabolism.
Expected Milestones	• Results from the Phase 1 clinical study of LYT-300 are expected in the second half of 2022 and will be used to inform the design of possible future studies evaluating LYT-300 in indications that could include depression, anxiety, sleep disorders, fragile X tremor-associated syndrome, essential tremor and epileptic disorders, among others.
Intellectual Property	• Within the extensive Glyph intellectual property portfolio, which covers a wide range of novel linker chemistries, LYT-300 is specifically covered by four patent families comprising one international PCT application, seven foreign patent applications, and six U.S. patent applications as of December 31, 2021, two of which families are co-owned with Monash University and two of which are PureTech owned. Any patents to issue from these patent applications are expected to expire in 2039 or 2042, exclusive of possible patent term adjustments or extensions or other forms of exclusivity.

LYT-300 Program

Therapeutic Candidate[1]	Indication	Discovery	Preclinical	Phase 1	Phase 2	Phase 3
LYT-300 Oral Allopregnanolone	Neurological and neuropsychological conditions					

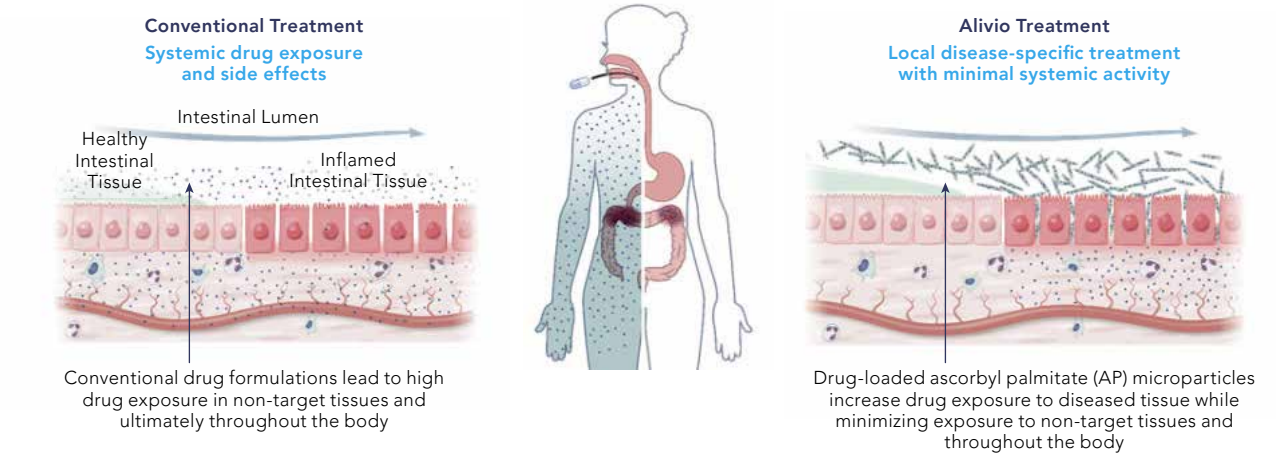
Phase completed Phase in progress

LYT-510, LYT-500

Therapeutic Candidate[1]	PureTech Ownership	Indication	Stage of Development
LYT-510	Wholly-owned	Inflammatory bowel disease and chronic pouchitis	Preclinical
LYT-500	Wholly-owned	Inflammatory bowel disease	Preclinical

- LYT-510 is our lead candidate generated from our Alivio™ technology platform and is an oral inflammation-targeting formulation of tacrolimus, a potent immunosuppressant drug, in development to treat inflammatory bowel disease (IBD) and chronic pouchitis. While tacrolimus is FDA-approved for certain indications, it has been evaluated in several clinical studies as a potential treatment for IBD, where it has demonstrated strong efficacy with high response and remission rates. However, despite the compelling efficacy, IBD patients are at risk for significant side effects due to systemic exposure, which has prevented tacrolimus' advancement for these indications. We believe that our oral formulation that targets tacrolimus to inflamed tissue, with minimal systemic exposure to healthy tissues, can overcome these limitations to potentially provide a safe and effective oral treatment for IBD patients. More broadly, this approach offers a path to unlocking the full therapeutic potential of multiple immunosuppressant and anti-inflammatory drugs that have well established clinical efficacy in a way that matches the chronic, variable expression of autoimmune diseases.
- LYT-500 is an oral combination therapy in development for IBD. Using our Alivio technology platform, we have combined two active agents into a single therapeutic candidate designed to enhance the local treatment and healing of inflamed tissues, while minimizing systemic exposure of these agents.

Inflammation-Targeting Immunomodulation Platform



Key Points of Innovation & Differentiation

- Using our Alivio technology platform, a biologic agent and/or small molecule drug can be administered in an oral dosage form that offers the potential to selectively act at the inflamed tissues locally to maximize efficacy, while minimizing toxicity by reducing systemic exposure of the drugs.
- LYT-510 is an oral inflammation-targeting formulation of tacrolimus in development to treat IBD and chronic pouchitis. Tacrolimus is a potent immunosuppressant drug that is FDA approved for prophylaxis of organ rejection in patients receiving allogeneic kidney, liver or heart transplants and topically for the treatment of atopic dermatitis. Clinical studies have demonstrated that tacrolimus can be an effective agent to induce remission in IBD patients following a short-term treatment regimen. However, the current tacrolimus products have found limited use because of a narrow therapeutic window, which has the potential to cause various systemic side effects including hypertension, paresthesia, neuropathy, renal impairment, and opportunistic infections. We believe that LYT-510 can overcome these clinical challenges by targeting tacrolimus to inflamed intestinal tissue and minimizing systemic exposure. With this enhanced PK profile, we believe that LYT-510 has the potential to be the first tacrolimus treatment approved for IBD in the U.S.
- LYT-500 is an oral therapeutic candidate in development for the potential treatment of mucosal barrier damage in people with IBD. It contains a unique combination of IL-22 and an immunosuppressant drug, which is designed to address the two key underlying causes of IBD pathogenesis and progression, namely mucosal barrier disruption and inflammation. Unlike many therapies in development for IBD, LYT-500 is designed with a dual mechanism of action to provide both mucosal repair and targeted resolution of tissue inflammation, which are critical for optimal disease management.

Program Discovery Process by the PureTech Team

- A key challenge faced in developing new drugs for the treatment of autoimmune and inflammatory disease is that attractive drug targets are frequently expressed in both diseased and normal tissue. Consequently, we are interested in identifying ways to address autoimmune disease in a more targeted manner. We have been inspired by the key observation that pathologic inflammation driven by dysfunctional immune signaling frequently manifests at specific sites in tissues and organs. However, the current treatments and therapeutic approaches act broadly to suppress the immune system throughout the body. This mismatch substantially limits the potential targets that can be pursued due to narrow therapeutic windows. Moreover, combining therapies to address multiple aspects of the autoimmune diseases is quite challenging due to both distinct and overlapping drug toxicity profiles. Working with leading scientists, we identified and in-licensed a technology platform in May 2016 that was created by Jeffrey Karp, Ph.D., Professor of Medicine at Harvard Medical School and Brigham and Women's Hospital, and Robert Langer, Sc.D., David H Koch Institute Professor at MIT. As demonstrated in multiple publications, our Alivio technology platform can be used to develop therapeutic candidates that selectively target inflamed tissues and release drugs in proportion to the severity of inflammation.

Patient Need & Market Potential

- IBD is estimated to affect approximately 3.9 million people in the U.S.[2], with monoclonal antibody therapies being the preferred treatment option for patients with moderate-to-severe disease. However, these therapies must be provided through multiple injections over time and are associated with several limitations including a lack of efficacy for some patients, dose-limiting AEs, loss of efficacy over time via anti-drug antibody development and the potential for opportunistic infections or malignancies.
- We believe that an ideal solution for treating IBD and chronic pouchitis would be an oral drug therapy that targets multiple mechanisms of disease pathogenesis while minimizing the potential for systemic side effects. We believe LYT-510 and LYT-500, developed from our Alivio technology platform, can potentially fulfill this goal.

1 The FDA and corresponding regulatory authorities will ultimately review our clinical results and determine whether our wholly-owned therapeutic candidates are safe and effective. No regulatory agency has made any such determination that LYT-510 or LYT-500 are safe or effective for use by the general public for any indication.

2 Inflammatory Bowel Disease (IBD) in the United States. (2021, November 09). https://www.cdc.gov/ibd/data-statistics.htm

Milestones Achieved & Development Status	• In multiple preclinical IBD models, LYT-510 showed significant improvements in several efficacy endpoints compared to untreated controls. Furthermore, the inflammation-targeting properties were shown to result in very low systemic blood levels compared to the current immunosuppressant formulations, which minimizes the potential for systemic side effects. • In 2020, the U.S. Department of Defense (DOD) Technology/Therapeutic Development awarded $3.3 million to support the advancement of LYT-510 into the clinic. • Progress in the preclinical development of LYT-500 is demonstrated by the following achievements: – We have developed an inflammation-targeting IL-22 composition with analytical data to support high IL-22 loading, high encapsulation efficiency, preservation of biologic activity, enzyme-mediated drug release and stability in simulated intestinal fluids. In addition, we have a comparable data set for an inflammation-targeting composition that combines IL-22 with an immunosuppressant drug. – We have completed initial preclinical evaluation of an inflammation-targeting IL-22 composition in a preclinical IBD model, where we demonstrated improvement in multiple endpoints related to mucosal healing. – We have demonstrated efficacy of the inflammation-targeting drug combination in a rodent IBD model, with improvements observed across several endpoints related to mucosal healing and inflammation. – We have developed oral dosage forms to enable preclinical testing of the inflammation-targeting IL-22 alone and in combination with an immunosuppressant drug and have initiated animal studies to evaluate their efficacy.
Expected Milestones	• We intend to file for regulatory approval to initiate first-in-human studies at year end 2022 and initiate a clinical study evaluating LYT-510 as a single agent for the potential treatment of IBD and chronic pouchitis in early 2023. • We expect preclinical proof-of-concept data for LYT-500 in the first half of 2022.
Intellectual Property	• The intellectual property portfolio supporting LYT-510 and LYT-500 consists of coverage around both the broader inflammation-targeting platform and the specific drug combination candidate. Platform intellectual property is supported by one patent family that has been exclusively licensed from the Brigham and Women's Hospital, which includes seven issued patents to date and five pending applications within and outside the U.S. In addition, intellectual property specific to the LYT-510 and LYT-500 candidates includes two patent families which are owned by Alivio that consist of 13 patent applications within and outside the U.S.

LYT-510 and LYT-500 Programs

Therapeutic Candidate[1]	Indication	Discovery	Preclinical	Phase 1	Phase 2	Phase 3
LYT-510 Oral Immunosuppressant	IBD/Chronic pouchitis					
LYT-500 Oral IL-22 + Immunosuppressant	IBD					

Phase completed Phase in progress

LYT-503/IMB-150

Therapeutic Candidate[1]	PureTech Ownership	Indication	Stage of Development
LYT-503/IMB-150 (Partnered program)	Wholly-owned (licensed)	Interstitial cystitis/bladder pain syndrome	Preclinical

- LYT-503/IMB-150 is being advanced through a collaboration with Imbrium Therapeutics for the potential treatment of IC/BPS. LYT-503/IMB-150 was developed using our Alivio technology platform, which involves selectively restoring immune homeostasis at inflamed sites in the body while reducing their impact on the rest of the body's immune system. This long sought-after approach has the potential to broadly enable new medicines to treat a range of chronic and acute inflammatory disorders, including drugs whose use has been limited due to issues of systemic toxicity or problematic PK profiles.

Key Points of Innovation & Differentiation

- To achieve our vision of selective immunomodulation, we are advancing our proprietary Alivio technology platform centered on a class of self-assembling therapies that selectively bind to inflamed tissue. The platform allows for the development of inflammation-targeting therapeutic candidates using a wide array of active pharmaceutical ingredients, or APIs, including small molecules, biologics and nucleic acids. Using this technology, LYT-503/IMB-150 is designed to provide local therapy at the inflamed lesions along the bladder surface of IC/BPS patients while minimizing the potential for related systemic toxicities.

Program Discovery Process by the PureTech Team

- A key challenge in new drug development for autoimmune and inflammatory disease is that attractive drug targets are frequently expressed in both diseased and normal tissue. Consequently, we were interested in identifying ways to address autoimmune disease in a targeted manner such that healthy cells and tissues are not impacted by the drug. We were inspired by the key observation that pathologic inflammation frequently manifests at specific sites in tissues and organs and is driven by dysfunctional immune signaling. However, traditional approaches act broadly to suppress the immune system throughout the body affecting both the disease and healthy tissues. The current approaches therefore substantially limit the potential targets that can be pursued due to narrow therapeutic windows. Working with leading scientists, we identified and in-licensed a technology platform in May 2016 that was created by Jeffrey Karp, Ph.D., Professor of Medicine at Harvard Medical School and Brigham and Women's Hospital, and Robert Langer, Sc.D., David H Koch Institute Professor at MIT. As demonstrated in multiple publications, our Alivio technology platform can be used to develop therapeutic candidates that selectively target inflamed tissues and release drugs in proportion to the severity of inflammation.

Patient Need & Market Potential

- IC/BPS is a chronic bladder condition that consists of discomfort or pain in the bladder or surrounding pelvic region and is often associated with frequent urination. It is estimated to affect four million to 12 million people in the U.S. Current treatments fail to control pain in many patients.

Milestones Achieved & Development Status

- In December 2018, we entered into an option and license agreement with Imbrium Therapeutics to advance LYT-503/IMB-150 through clinical development and potential commercialization as a treatment for IC/BPS.
- In August 2021, we announced that Imbrium Therapeutics had exercised its license option to develop LYT-503/IMB-150. PureTech received an option exercise payment of $6.5 million and is eligible to receive up to $53 million in additional development milestone payments for this program and royalties on potential product sales.

Expected Milestones

- Imbrium is planning to file an IND application for LYT-503/IMB-150 in 2022.

Intellectual Property

- The intellectual property portfolio supporting LYT-503/IMB-150 consists of coverage around both the Alivio technology platform and the drug candidate. Platform intellectual property is supported by one patent family, which has been exclusively licensed from the Brigham and Women's Hospital and includes seven issued patents and two pending applications within and outside the U.S. Intellectual property specific to the LYT-503/IMB-150 candidate. In addition, the LYT-503/IMB-150 IP includes one patent family which is owned by Alivio that consists of two issued patents and five applications within and outside the U.S.

LYT-503/IMB-150 Program

Therapeutic Candidate[1]	Indication	Discovery	Preclinical	Phase 1	Phase 2	Phase 3
LYT-503/IMB-150 (Partnered program) Non-opioid	Interstitial cystitis/bladder pain syndrome (IC/BPS)					

Phase completed Phase in progress

1 The FDA and corresponding regulatory authorities will ultimately review our clinical results and determine whether our wholly-owned therapeutic candidates are safe and effective. No regulatory agency has made any such determination that LYT-503/IMB-150 is safe or effective for use by the general public for any indication. On July 23, 2021, Imbrium Therapeutics exercised its option to license LYT-503/IMB-150 pursuant to which it is responsible for all future development activities and funding for LYT-503/IMB-150.

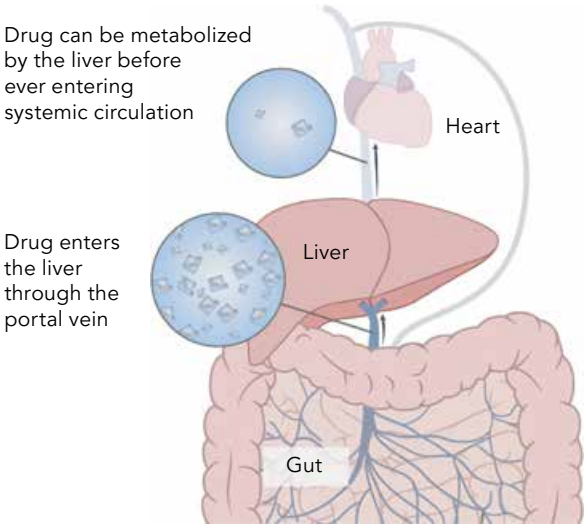
Glyph™: Lymphatic Targeting Chemistry Platform

Therapeutic Candidate	PureTech Ownership	Description
Glyph Technology Platform	Wholly-owned	Lymphatic-targeting chemistry platform leveraging the body's natural lipid absorption and transport process to orally administer drugs via the lymphatic system

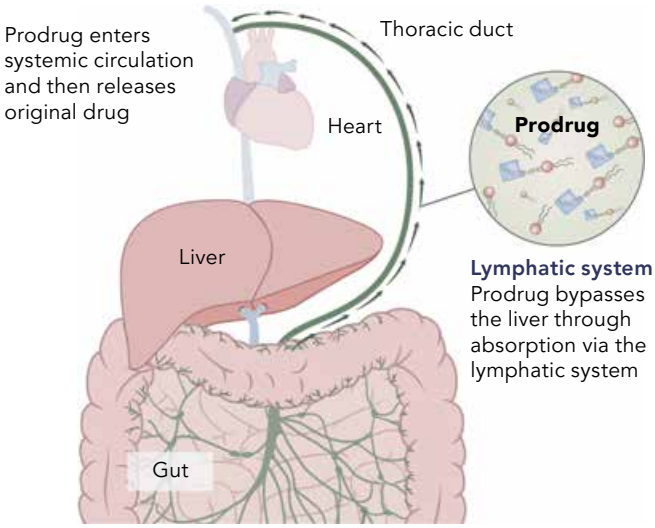
- We are advancing a synthetic lymphatic-targeting chemistry platform called Glyph, which is designed to employ the lymphatic system's natural lipid absorption and transport process and has led to the nomination of LYT-300 for continued expansion of our Wholly Owned Pipeline. Consumed nutrients and most orally administered pharmaceuticals are initially absorbed by the small intestine mucosa, distributed to the liver by the portal vein before entering systemic circulation. Importantly, many consumed dietary lipids, particularly triglycerides, enter systemic circulation by an alternate route. Triglycerides, which are composed of three fatty acid chains tethered to a 3-carbon glycerol molecule, are absorbed by small intestine mucosal enterocytes where they are incorporated into large lipid-protein complexes (chylomicrons) and released into the submucosa. Chylomicrons are too large to enter blood vessels and are instead taken up by submucosal lymphatic vessels. Once in the lymphatic vessels, they are transported to mesenteric lymph nodes associated with the GI tract where they pass into larger lymphatic vessels connected to the thoracic duct, then merge with systemic circulation as illustrated in the figure below on the right. This is in contrast to conventional systemic circulation via the gut and liver as shown in the figure below on the left.

Glyph: A synthetic lymphatic-targeting chemistry platform

Conventional oral drug transport



Glyph oral drug transport via the lymphatic system



- Our proprietary Glyph technology platform takes advantage of the fact that one of the triglyceride-associated fatty acids remains bound to dietary lipids during intestinal absorption, chylomicron conversion, lymphatic vessel uptake and eventual transport into the circulatory system. Using a modular set of proprietary chemical entities, small molecule pharmaceutical compounds can be attached to triglycerides where, following oral administration, the small molecule is directed into the mesenteric lymphatic system and on to systemic circulation. The process of drug release from the triglyceride is governed by self-cleaving chemical structures, with different release-timing features, that tether the small molecule to the module connected to the triglyceride. The figure below is a representation of the proprietary chemistry for the design of our lymphatic targeting technology. The active pharmaceutical ingredient (API) is meant to indicate an example of a pharmaceutical small molecule that is attached to the triglyceride group (Glyceride in the figure on the next page) using proprietary linker chemistry (linker in the figure on the next page) to create a prodrug of the API. The prodrug also includes a proprietary self-immolative or cleaving chemistry (SI in the figure on the next page) that can be tuned to release the API in its intact original form.

Key Points of Innovation & Differentiation

- We believe this platform provides the following capabilities:
  - Targeting the mesenteric lymphatics: This lymphatic targeting technology has important features that offer potential advantages in the creation of orally-administered medicines, especially those that need to reach immune system drug targets present in the GI tract mucosa and submucosa, such as intestine-associated immune cells, or in the mesenteric lymphatic vasculature, such as circulating immune cells, and mesenteric lymph nodes, such as lymph node stromal cells, antigen-presenting cells and lymph node-associated immune cells.
  - Enabling and enhancing oral bioavailability by bypassing first-pass metabolism: We believe this technology could provide a broadly applicable modular means to potentially enable oral administration of a range of bio-active natural molecules, such as neurosteroids, cannabinoids, and a large number of parenterally administered drugs, that are otherwise not orally bioavailable. This technology also has the potential to significantly enhance the bioavailability of orally-administered drugs that suffer from substantial first-pass hepatic metabolism, especially those utilized in combination therapies, that act as modulators (inducers and/or inhibitors) of drug-metabolizing systems in the liver.

Program Discovery Process by the PureTech Team

- We sought out different approaches that could selectively traffic therapeutic molecules through the lymphatic system to target immune cells in the lymph nodes. Based on insights gained internally and via unpublished findings through our network of collaborators, we became aware of certain technology being developed at Monash University that had the potential to selectively target the lymphatic system. We obtained an exclusive license to this technology and the related intellectual property from Monash University. We have since further developed the platform and have generated our own intellectual property associated with the Glyph technology platform.
- We have developed an oral lipid prodrug of natural allopregnanolone, LYT-300, which is our first therapeutic candidate derived from our Glyph platform designed to treat a range of neurological and neuropsychological conditions such as depression, anxiety, sleep disorders, fragile X tremor-associated syndrome, essential tremor and epileptic disorders, among others.

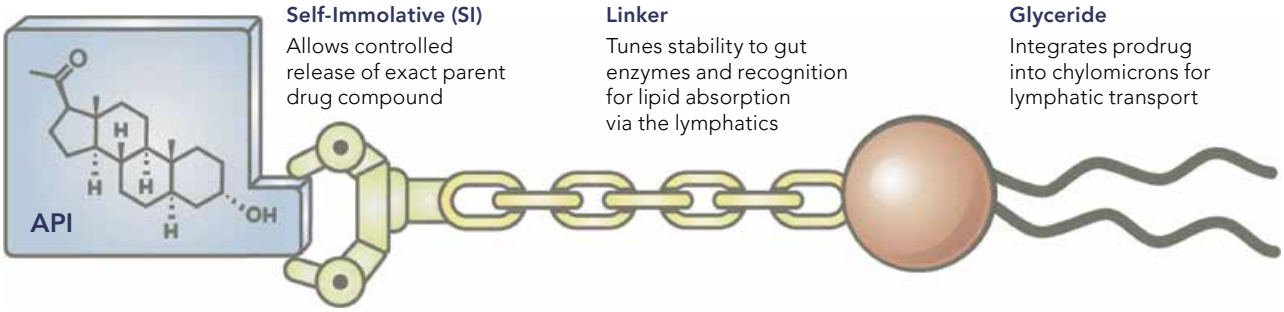
Milestones Achieved & Development Status

- In September 2021, preclinical proof-of-concept research was published in *Nature Metabolism*, which provides further support for the therapeutic potential of our Glyph technology platform[1]. The study showed for the first time that restoring normal function of the mesenteric lymphatics may reverse insulin resistance and modify obesity-associated metabolic disease. The study also found that inhibition of COX-2 and VEGF-C signaling within the mesenteric lymphatics resulted in a repatterning of the lymphatic vasculature, which in turn led to reduced branching and significantly less leakage of lymphatic fluids rich in lipids and pro-inflammatory mediators. Targeted inhibition of COX-2 function with a celecoxib prodrug developed using our lymphatic targeting Glyph technology platform led to a normalization of multiple biomarkers, including VEGF-C concentrations specifically within mesenteric lymph and surrounding adipose tissue, and to levels observed in control animals that were not fed a high-fat diet. This correlated with reduced lymphatic vessel branching and leakage as well as restoration of glycemic control, and weight gain was blocked in the animals fed a high-fat diet. In fact, targeted administration of the celecoxib Glyph prodrug led to a 10-fold greater uptake of celecoxib in mesenteric lymph and more effective restoration of lymphatic function and glycemic control compared to the administration of unmodified celecoxib, which is commercially available.
- In February 2021, preclinical proof-of-concept for our Glyph technology platform was published in the *Journal of Controlled Release*[2]. The additional results highlighted in the publication support the ability of the platform to target administration of drugs such as mycophenolic acid (MPA), an immunosuppressant, into lymph and directly into gut-draining mesenteric lymph nodes (MLNs). As a key nexus of immune cell trafficking, MLNs play major roles in the pathophysiology of a range of conditions including inflammatory and autoimmune diseases, cancer and metabolic diseases. As published, oral administration of a Glyph-based prodrug of MPA (Glyph-MPA) resulted in a >80-fold increase in uptake of total MPA into the lymphatic system and a >20-fold increase in MPA concentrations in MLNs relative to what was achieved with oral dosing of free MPA. Furthermore, MPA administered orally as Glyph-MPA was significantly more potent than free MPA in inhibiting T cell proliferation in mice challenged with antigen. Plasma levels were similar with Glyph-MPA and MPA, indicating low potential for the emergence of new systemic side effects. Additionally, a prodrug of a fluorescent tracer was shown to rapidly accumulate in MLNs following administration. Together, these findings provide further support of the potential of our Glyph technology for oral administration of small molecule drugs directly to the lymphatic system, including drugs with immunomodulatory properties.
- In the April 2022 post-period, preclinical proof-of-concept research was published in *Frontiers in Pharmacology*, which demonstrated our Glyph platform can enhance the oral bioavailability of buprenorphine, a clinically-validated opioid replacement therapy, further expanding the range of clinically-validated drug classes shown to be amendable to the Glyph technology.
- We have successfully extended our lymphatic targeting platform to encompass more than 20 molecules as well as a range of novel linker chemistries that have demonstrated promising lymphatic targeting in preclinical studies. We expect to select therapeutic candidates from this and ongoing discovery work.
- We believe the Glyph technology platform could provide a broadly applicable modular means to potentially enable oral administration of a range of bio-active natural molecules, such as neurosteroids, cannabinoids and a large number of parenterally administered drugs that are otherwise not orally bioavailable, or such as orally-administered drugs that suffer from substantial first-pass hepatic metabolism or those drugs, especially those utilized in drug combination therapies, that act as modulators (inducers and/or inhibitors) of drug-metabolizing systems in the liver. To demonstrate the utility of our Glyph lipid prodrug platform, we chose a natural bio-active neurosteroid allopregnanolone as the subject of our inquiry, which has resulted in the LYT-300 program. However, we believe that this benefit has the potential to be widely applied to nearly any natural molecules or therapeutic compatible with the synthetic approach which suffers from hepatic first-pass metabolism as has been evaluated by us and our collaborators.

Intellectual property

- We have broad intellectual property coverage for our proprietary Glyph technology platform, which includes exclusively licensed and co-owned patent applications, as well as company-owned patent applications. These patent applications cover compositions of matter, methods of use and methods of treatment encompassing specific chemical modifications, including a wide range of novel linker chemistries, as well as various classes of lymphatic targeting therapeutics, which include prodrugs for a large number of APIs, for use in the treatment of a wide range of diseases and disorders. The most advanced of these is LYT-300, which is an oral form of FDA-approved allopregnanolone, a natural neurosteroid, that we believe may be applicable to a range of neurological conditions.
- As of December 31, 2021, our Glyph technology platform intellectual property portfolio consists of 17 patent families comprising 19 U.S. patent applications, 20 foreign patent applications and three foreign patents. Of these, company-owned intellectual property consists of nine U.S. patent applications in nine patent families. We exclusively licensed and co-own a patent portfolio of eight patent families comprising 33 U.S. and foreign patent applications and three foreign patents from Monash University. Any patents to issue from the in-licensed patent applications are expected to expire in 2035-2036 and any issued patents from the co-owned and company-owned patent applications are expected to expire in 2038-2042, exclusive of possible patent term adjustments or extensions or other forms of exclusivity.

Schematic representation of our lymphatic targeting prodrug technology



1 Cao, E., Watt, M.J., Nowell, C.J. et al. Mesenteric lymphatic dysfunction promotes insulin resistance and represents a potential treatment target in obesity. Nat Metab 3, 1175–1188 (2021). https://doi.org/10.1038/s42255-021-00457-w

2 Kochappan, R., Cao, E., Han, S., Hu, L., Quach, T., Senyschyn, D., Ferreira, V. I., Lee, G., Leong, N., Sharma, G., Lim, S. F., Nowell, C. J., Chen, Z., von Andrian, U. H., Bonner, D., Mintern, J. D., Simpson, J. S., Trevaskis, N. L., Porter, C. J. H. (2021). Targeted delivery of mycophenolic acid to the mesenteric lymph node using a triglyceride mimetic prodrug approach enhances gut-specific immunomodulation in mice. Journal of Controlled Release, 332, 636–651. https://doi.org/10.1016/j.jconrel.2021.02.008

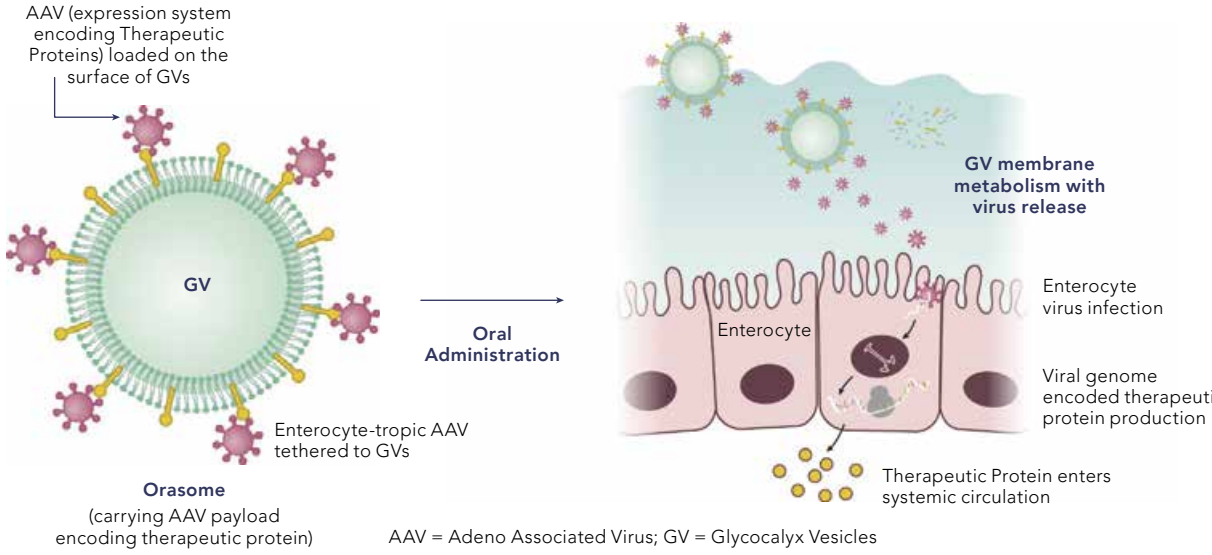
Orasome™ and Other Technology Platforms for Oral Administration of Therapeutics

Therapeutic Candidate	PureTech Ownership	Description
Orasome Technology Platform	Wholly-owned	Programmable and scalable approach for oral administration of nucleic acids and other biologics

- We are developing versatile and programmable oral biotherapeutics approaches, such as Orasome technology, to potentially enable the oral administration of macromolecule therapeutic payloads, including antisense oligonucleotides, short interfering RNA, mRNA, modular expression vector systems, peptides and nanoparticles that are otherwise administered exclusively by injection.
- Our Orasome technology platform was inspired by the in vivo trafficking of ubiquitous, naturally occurring extracellular vesicles, which are often referred to as exosomes or ectosomes, and we have engineered them for transport through the GI tract. We believe human cell-isolated exosomes/ectosomes have promise as vehicles for systemic drug administration due to their observed tolerability over synthetic polymer-based administration technologies. However, the fragile nature of exosomes/ectosomes from human cells limits their usage for oral administration and the type of post-isolation manipulations that can be applied in order to optimize such vesicles for exogenous drug cargo loading and storage.
- Our Orasome technology platform, for example, utilizes both synthetic and naturally occurring components isolated from multiple sources to yield glycocalyx-stabilized vesicles (GVs). We have engineered and formulated these vesicles to remain stable following oral consumption and transit through the upper GI tract. Orasome GVs are readily amenable to manufacturing at scale and at relatively low cost based on the accessibility of the various components and simplicity of assembly.

Orasome Technology

The figure below depicts one of the approaches we are exploring for the administration of oral biotherapeutics:



AAV = Adeno Associated Virus; GV = Glycocalyx Vesicles

- Our Orasome GVs are being engineered to transport macromolecular medicines to selected mucosal cell types of the intestinal tract where the therapeutics act either directly in the GI tract, transit through the mucosa to the underlying lymphatic vascular network or, in the case of cargos that yield mRNAs, enable the body to produce its own therapeutic proteins and peptides, such as antibodies within mucosal cells that are secreted into the mucosal lymphatic vascular network for subsequent systemic distribution. Using our Orasome technology platform, we believe it may be possible for a patient to take an oral drug product that will permit their own GI tract cells to make virtually any type of therapeutic protein. We believe this approach also has the potential to provide a more convenient and significantly less expensive means to administer biological medicines.
- In addition to Orasomes, we are also exploring the use of other approaches, such as certain exosomes isolated from milk as well as synthetic novel polymers and vesicles for delivering biotherapeutics.

Key Points of Innovation & Differentiation

- Our proprietary oral administration technology, such as our Orasome technology platform, has the potential to transform the treatment paradigm for diseases such as rheumatoid arthritis, diabetes, other autoimmune diseases and cancer for which the standard of care often requires intravenous infusion or subcutaneous injection of monoclonal antibodies (e.g., anti-PD-1, anti-tumor necrosis factor) or therapeutic proteins/peptides (e.g., glucagon-like peptide-1, insulin, granulocyte colony-stimulating factor GCSF, Factor VIII and IX, cytokines and erythropoietin), among others.

PureTech is well-positioned to unleash the potential of oral biotherapeutics

Limitations of protein-based therapeutics

- **Intravenous or subcutaneous administration** (infusion reactions, barrier for repeat dosing)
- **Lengthy scale-up timeline**

Limitations of mRNA-based therapeutics and vaccines

- **Intravenous, intramuscular or subcutaneous administration** (infusion reactions, co-medications needed for dosing, very limited repeat dose options)
- **Formulation-based immune and cellular toxicities** (protein synthesis by liver hepatocytes)
- **High dose requirement for protein production**

Potential advantages of the Orasome™ technology platform:

- **Orally administered** (flexible repeat dosing)
- **Body manufactures the therapeutic proteins**
- **Very low immune and cell toxicity** (protein synthesis in GI tract)
- **Low dose requirement for protein production**

Program Discovery Process by the PureTech Team

- We sought out different approaches to enable the oral administration of macromolecule therapeutic payloads that are otherwise administered exclusively by injection. We have independently developed our Orasome technology platform and have generated data and intellectual property supporting oral administration of macromolecule therapeutic payloads. We are also developing other oral administration technologies and intellectual property.

Milestones Achieved and Development Status

- In 2021, we established preclinical proof-of-concept supporting the potential of the Orasome technology platform to achieve production of therapeutic proteins in the gut of an animal following simulated oral administration of expression systems and transport of these proteins from the gut into systemic circulation. Proof-of-concept was observed with multiple formulations involving Orasome technology which are being further optimized to achieve a range of expression profiles for therapeutic proteins.

Expected Milestones

- We expect to generate additional data in 2022, with Orasomes and other technologies, across a range of preclinical models and therapeutic proteins. We expect to generate data to demonstrate that oral administration of Orasomes, carrying an expression system for a desired therapeutic protein, can achieve therapeutic levels of the protein in multiple species of preclinical models with achievement of safe repeat-dose administration.
- This work could lay the foundation for IND-enabling clinical studies for one or more additional therapeutic candidates to be included in our Wholly Owned Pipeline. We intend to leverage our proprietary technology platforms, such as orasomes, as well as our extensive network with major pharmaceutical companies and world-leading scientists, to generate additional novel therapeutic candidates.

Intellectual Property

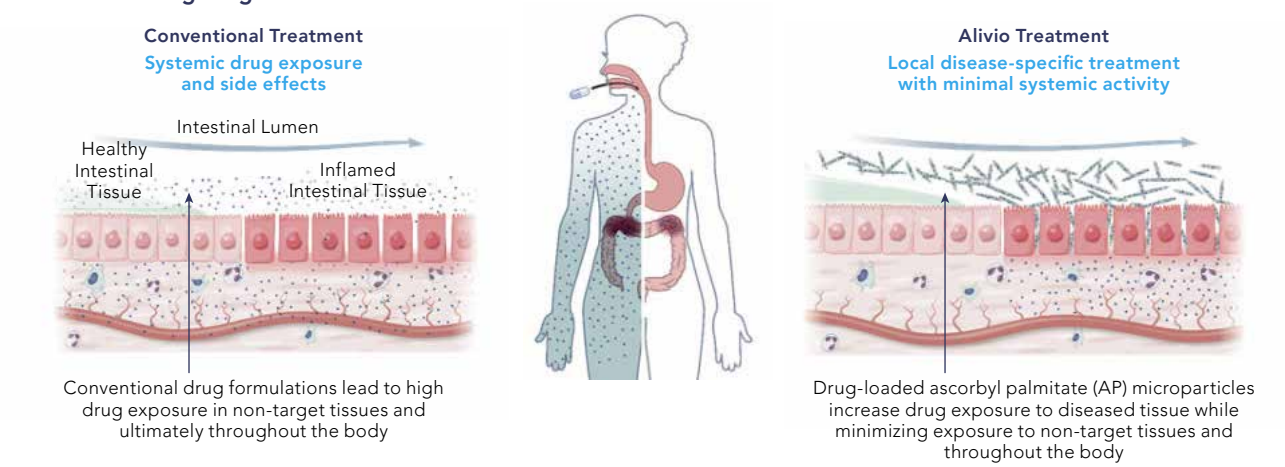
- We have broad intellectual property coverage for our Orasome technology platform. Our Orasome technology platform intellectual property portfolio covers compositions of matter, methods of use and methods of treatment spanning various platform-based technologies, as well as various broad classes of Orasome-formulated therapeutics, which include nucleic acid-based therapeutics (such as messenger RNA, short interfering RNA and antisense oligonucleotide-based approaches), small molecules, biologics (such as peptides, proteins and antibodies), expression systems for biologics and other therapeutics for use in the treatment of a wide range of diseases and disorders, including various immunological disorders, such as cancers and inflammatory diseases.
- As of December 31, 2021, PureTech's Orasome technology platform patent portfolio consists of four U.S. and nine foreign patent applications and one pending international PCT application in five patent families. Any patents to issue from these patent applications are expected to expire in 2037 through 2041, exclusive of possible patent term adjustments or extensions or other forms of exclusivity.
- With regards to milk exosomes, we exclusively licensed a patent portfolio consisting of two patent families from 3P Biotechnologies, Inc., based on certain milk exosome technology originating from the University of Louisville. We also exclusively licensed a patent portfolio consisting of two patent families from NuTech Ventures, based on certain milk extracellular vesicle technology originating from the University of Nebraska.

Alivio™ Technology Platform

Therapeutic Candidate	PureTech Ownership	Description
Alivio Technology Platform	Wholly-owned	Pioneering inflammation-targeted disease immunomodulation

- Using our Alivio technology platform, we are pioneering inflammation-targeted disease immunomodulation, which involves selectively restoring immune homeostasis at inflamed sites in the body, while having the potential for minimal impact on the rest of the body's healthy tissues, as a novel strategy to more effectively treat a range of chronic and acute inflammatory disorders. This long sought-after approach has the potential to broadly enable new medicines to treat a range of chronic and acute inflammatory disorders, including drugs that were previously limited by issues of systemic toxicity or undesirable PK.

Inflammation-Targeting Immunomodulation Platform

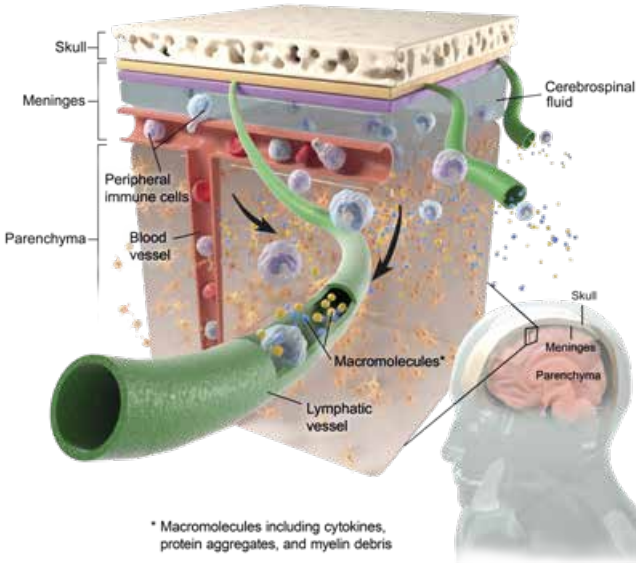


Key Points of Innovation & Differentiation	• To achieve our vision of selective immunomodulation, we are advancing our Alivio technology platform centered on a class of self-assembling therapies that selectively bind to inflamed tissue. The platform allows for the development of inflammation-targeting therapeutic candidates using a wide array of active pharmaceutical ingredients (APIs) including small molecules, biologics and nucleic acids. Using this technology, we can design therapeutic candidates that have the potential to treat autoimmune diseases locally at the site of inflammation while avoiding systemic toxicities.
Program Discovery Process by the PureTech Team	• A key challenge in new drug development for autoimmune and inflammatory disease is that attractive drug targets are frequently expressed in both diseased and normal tissue. Consequently, we were interested in identifying ways to address autoimmune disease in a targeted manner such that healthy cells and tissues are not impacted by the drug. We were inspired by the key observation that pathologic inflammation frequently manifests at specific sites in tissues and organs and is driven by dysfunctional immune signaling. Traditional approaches act broadly to suppress the immune system throughout the body affecting both the disease and healthy tissues. The current approaches therefore substantially limit the potential targets that can be pursued and frequently result in narrow therapeutic windows. Working with leading scientists, we identified and in-licensed a technology platform in May 2016 that was created by Jeffrey Karp, Ph.D., Professor of Medicine at Harvard Medical School and Brigham and Women's Hospital, and Robert Langer, Sc.D., David H Koch Institute Professor at MIT. As demonstrated in multiple publications, our Alivio technology platform can be used to develop therapeutic candidates that selectively release drugs at inflamed sites of targeted tissues and spares healthy tissues.
Patient Need & Market Potential	• Preclinical results suggest our Alivio technology platform could be applied to diseases such as IBD, inflammatory arthritis, organ transplantation and IC/BPS. These diseases collectively impact tens of millions of patients in the U.S. alone and have limited treatment options. IC/BPS is a chronic bladder condition that consists of discomfort or pain in the bladder or surrounding pelvic region and is often associated with frequent urination. It is estimated to affect four million to 12 million people in the U.S. Current treatments fail to control pain in many patients. IBD is estimated to affect approximately 3.9 million people in the U.S.
Milestones Achieved & Development Status	• In August 2021, we announced that Imbrium exercised a license option under the companies' research and development collaboration agreement to develop LYT-503/IMB-150. In connection with the option exercise, we received an upfront payment of $6.5 million and are eligible to receive up to $53 million in additional development milestone payments for this program as well as royalties on product sales. • Using our Alivio technology platform, we are developing LYT-510, an oral inflammation-targeting formulation of tacrolimus, a potent immunosuppressant drug, to treat IBD and chronic pouchitis, LYT-500, an oral combination therapy for the treatment of IBD, and LYT-503/IMB-150, our therapeutic candidate being advanced in collaboration with Imbrium Therapeutics for the potential treatment of IC/BPS.
Expected Milestones	• We intend to file for regulatory approval to initiate first-in-human studies at year end 2022 and initiate a clinical study evaluating LYT-510 as a single agent for the potential treatment of IBD and chronic pouchitis in early 2023. • We expect preclinical proof-of-concept data for LYT-500 in the first half of 2022. • Imbrium is planning to file an IND application for LYT-503/IMB-150 in 2022. • We are evaluating other potential therapeutic candidates leveraging Alivio technology platform for Wholly Owned Pipeline expansion.
Intellectual Property	• Intellectual property portfolio covering the Alivio inflammation-targeting technology platform consists of six patent families. Collectively, across these patent families, there are 18 issued patents within and outside the U.S. with claims covering inflammation-targeting compositions, methods of making and methods of using as drug products. Within these families, there are a total of eight patent applications pending in the U.S. and foreign countries. All patents and patent applications covering the platform technologies have been obtained from the Brigham and Women's Hospital under an exclusive licensing agreement in all territories.

Meningeal Lymphatics Research Program

Therapeutic Candidate	PureTech Ownership	Description
Meningeal Lymphatics Research Program	Wholly-owned	Harnessing meningeal lymphatics to potentially treat a range of neurodegenerative and neuroinflammatory conditions

- The lymphatic system is an important part of the immune system, GI system and central nervous system, or CNS. Loss of lymphatic flow can play a critical role in diseases of these systems. The recent discovery of meningeal lymphatics in the brain, an area once thought to have immune privilege, has shed new light on neurodegenerative diseases and lymphatic vessel aging.



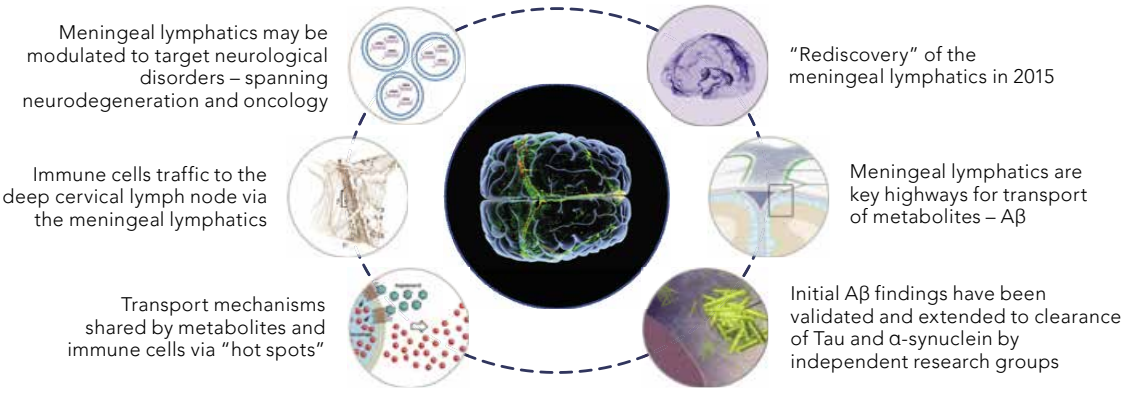
Key Points of Innovation & Differentiation

- Among the macromolecules that are drained via the lymphatics are pathogenic macromolecules such as amyloid-beta (Aβ) and tau, which are both associated with Alzheimer's disease, or AD, pathology, as well as alpha-synuclein, which is associated with Parkinson's disease. Blocking the lymphatic flow increases levels of these molecules in the brain. In animal models of AD, AD-associated tauopathies and Parkinson's disease, blockage of meningeal lymphatic flow significantly exacerbated disease progression and severity whereas improving flow through aged meningeal lymphatics improved cognitive function in these animal models. With aging, the lymphatic vessels that drain the brain become dysfunctional and no longer drain as efficiently. The "lymphedematous characteristics" of meningeal lymphatic vessels in aged animals might be leading to inefficient clearance of pathologic macromolecules and potentially increased risk for neurodegenerative diseases. Therefore, restoration of lymphatic flow may be a novel class of therapies for neurodegeneration associated with poor lymphatic drainage.

Program Discovery Process by the PureTech Team

- One of our academic collaborators discovered a functional lymphatic system in the meninges of the brain that forms the basis of our meningeal lymphatics research program. These meningeal lymphatics have been described as the "brain drain," a route through which macromolecules are flushed from the brain in cerebrospinal fluid. We believe that augmenting meningeal lymphatic vasculature function may potentially improve outcomes for a range of neurodegenerative and neuroinflammatory conditions that are not currently effectively treated.

CNS lymphatics: Harnessing an overlooked immune and metabolite transport network



Milestones Achieved & Development Status

- In April 2021, we announced the publication of preclinical research in *Nature*, suggesting that restoring lymphatic flow in the brain, either alone or in combination with passive immunotherapies such as antibodies directed at amyloid-beta, has the potential to address a range of neurodegenerative diseases, such as Alzheimer's and Parkinson's diseases, which potentially impairs the efficacy of passive immunotherapies such as amyloid-beta-targeting antibodies. The work also uncovered a link between dysfunctional meningeal lymphatics and damaging microglia activation in Alzheimer's disease, suggesting another route by which restoring healthy drainage patterns could improve clinical outcomes.

Intellectual Property

- We have broad intellectual property coverage around our meningeal lymphatics discovery research program, which includes exclusively licensed patent applications covering compositions of matter, methods of use and methods of treatment encompassing its platform-based brain lymphatic technologies, including the identification of macromolecular targets, as well as various classes of brain lymphatic targeting therapeutics for use in the treatment of a wide range of neurodegenerative and neuroinflammatory conditions, as well as various neuropathies and cancers.
- As of December 31, 2021, our meningeal lymphatics discovery research program patent portfolio consists of four patent families comprising six patent applications in U.S. and foreign countries, and two international PCT applications exclusively licensed from the University of Virginia Licensing & Ventures Group. Any patents to issue from the in-licensed patent applications are expected to expire in 2037 through 2041, exclusive of possible patent term adjustments or extensions or other forms of exclusivity.

PureTech's Founded Entities

Founded Entities

Founded Entity	PureTech Ownership[1]	Therapeutic Candidate[2]		Indication	Stage of Development	Royalties[3]
	5.6%	KarXT	P	Schizophrenia Alzheimer's disease psychosis	Phase 3 Phase 3 Ready	Royalties
	22.3%	Akili is pioneering the development of game-changing technologies to usher in a new era of congitive medicine. EndeavorRx®[4] (formerly known as AKL-T01) is the first FDA cleared and CE marked video game treatment. In the U.S., EndeavorRx is indicated to improve attention function as measured by computer-based testing in children ages 8-12 years old with primarily inattentive or combined-type ADHD, who have a demonstrated attention issue.				
	23.5%	Plenity®[5,6] Plenity® for adolescents[5] GS200[5] GS300[5] GS500[5]	D D D D	Weight management Adolescent weight management Weight management in T2D/prediabetes NASH/NAFLD Functional constipation	Commercial Pending Discussion with FDA[7] Clinical Trial Complete Clinical Pivotal	Royalties
	8.6%	VOR33 (CD33) VCAR33	B B	Acute myeloid leukemia Myelodysplastic syndromes, myeloproliferative neoplasms Bridge-to-transplant AML	Phase 1/2a Preclinical Phase 1/2	N/A
	41.4%	VE303 VE202 VE416 VE800 VE707	B B B B B	*C. difficile* IBD Food allergy Solid tumors Gram-negative infections	Phase 3 Ready Phase 2 Ready Phase 1/2 Phase 1 Preclinical	N/A
	76.0%	FOL-004	P/D	Androgenetic alopecia	Phase 3 Ready	Royalties
	44.6%	Sonde One for Respiratory[5] Sonde Mental Fitness[5]	D D	Respiratory risk detection and monitoring app Monitoring vocal features linked to depression, anxiety, and cognition	Commercial Release Commercial Release	N/A
entrega	74.3%	ENT-100	B	Oral delivery of biologics, vaccines and other drugs	Preclinical	N/A

The letters next to the therapeutic candidates denote whether the therapeutic candidate is a pharmaceutical product (P), biologic (B) or device (D).

1 Relevant ownership interests and references to equity ownership for Founded Entities contained in this strategic report (pages 2-72) were calculated on a diluted basis (as opposed to a voting basis) as of December 31, 2021, including outstanding shares, options and warrants, but excluding unallocated shares authorized to be issued pursuant to equity incentive plans. Vor Bio, Karuna and Gelesis ownerships were calculated on a beneficial ownership basis in accordance with SEC rules as of March 4, 2022 and February 15, 2022 and March 31, 2022, respectively.

2 With the exception of Plenity and EndeavorRx, candidates are investigational and have not been cleared by the FDA for use in the U.S.

3 PureTech Health has a right to royalty payments as a percentage of net sales.

4 Please see footnote 10 on page 6 for EndeavorRx® indication and overview.

5 These therapeutic candidates are regulated as devices and their development has been approximately equated to phases of clinical development.

6 Please see footnote 11 on page 7 for Important Safety Information about Plenity®.

7 Contingent on FDA review of the research plan.

KARUNA THERAPEUTICS

Founded Entity	PureTech Ownership[1]	Therapeutic Candidate[2,3]		Indication	Stage of Development
Karuna[4]	5.6%	KarXT[4]	P	Schizophrenia	Phase 3
			P	Alzheimer's disease psychosis	Phase 3 Ready

- Karuna is developing novel therapies with the potential to deliver transformative medicines for people living with psychiatric and neurological conditions, including schizophrenia and dementia-related psychosis.
- KarXT (xanomeline-trospium) is an oral, investigational M1/M4-preferring muscarinic acetylcholine receptor agonist in development for the treatment of psychiatric and neurological conditions, including schizophrenia and psychosis in Alzheimer's disease (AD). KarXT combines xanomeline, a muscarinic receptor agonist, and trospium chloride, an FDA approved and well-established muscarinic receptor antagonist that has been shown not to measurably cross the blood-brain barrier. KarXT is designed to unlock the therapeutic potential of xanomeline, which demonstrated significant benefits in reducing symptoms of psychosis in Phase 2 studies in schizophrenia and AD, while ameliorating side effects seen in earlier studies. KarXT preferentially stimulates muscarinic receptors in the central nervous system implicated in these conditions, as opposed to current antipsychotic medicines, which bind to the D2 dopamine receptor. KarXT has the potential to usher in a new class of treatment for schizophrenia and dementia-related psychosis based on its differentiated mechanism of action.
- Xanomeline was previously evaluated by Eli Lilly and Company, or Eli Lilly, in randomized, double-blind, placebo-controlled trials in schizophrenia and AD. In the double-blind, placebo-controlled trial in AD, xanomeline demonstrated dose-dependent reductions in symptoms of psychosis and related behaviors, including hallucinations, delusions and agitation, as compared to patients on placebo, as measured by the Alzheimer's Disease Assessment Scale-Cognitive Subscale and the Clinician Interview-Based Impression of Change.
- Xanomeline is a muscarinic agonist that has demonstrated potential therapeutic benefit in schizophrenia and AD, yet its tolerability has been limited by side effects arising from muscarinic receptor stimulation in peripheral tissues, leading to nausea, vomiting, diarrhea and increased salivation and sweating, collectively referred to as cholinergic adverse events, or ChAEs, which led Eli Lilly to discontinue the clinical development of xanomeline. By pairing xanomeline with trospium chloride, Karuna believes KarXT could potentially maintain the therapeutic benefit of xanomeline while ameliorating its ChAEs.

Program discovery process by the PureTech team

- We were interested in developing a new approach to treat schizophrenia that was effective but did not have the debilitating side effects of the current class of antipsychotics, realizing that any potential new approaches could have wider applicability. We engaged with a group of leading schizophrenia experts who were most excited about muscarinic agonists, pointing to the data generated by Eli Lilly with xanomeline, which was not advanced at that time due to tolerability issues. We invented and broadly filed patents to cover the concept of combining a muscarinic receptor agonist with a peripherally acting antagonist, and we in-licensed xanomeline from Eli Lilly in May 2012. Andrew Miller, Ph.D., one of the core team members who was involved in running this program at PureTech, became Karuna's Chief Operating Officer, and we built a team of leading drug developers and neuroscientists around him, including Steven Paul, M.D., an expert in CNS drug discovery and development and now Karuna's Chief Executive Officer. Karuna completed an initial public offering on the Nasdaq Global Market in July 2019.
- Dr. Paul was formerly Executive Vice President for Science and Technology and President of the Lilly Research Laboratories at Eli Lilly and was involved in the original xanomeline work at Eli Lilly. Dr. Paul was also a Co-Founder of Sage Therapeutics and Voyager Therapeutics, where he served as Chief Executive Officer, as well as the former Scientific Director of the National Institute of Mental Health.

Patient need and market application

- Psychosis is a prominent and debilitating symptom that occurs in many neuropsychiatric disorders, including schizophrenia, dementia, bipolar disorder, major depressive disorder and inflammatory neurological diseases, such as multiple sclerosis, or MS. Despite its prevalence, there are no existing medicines that sufficiently and safely treat psychosis or cognitive impairments in people with schizophrenia.
- There are approximately 2.7 million adults living with schizophrenia in the U.S., of which approximately 40% are diagnosed with the disease, with around 1.2 million experiencing symptoms of psychosis. Antipsychotics are the mainstay therapy; however, drugs currently in use all rely on the same fundamental mechanism of action and, despite widespread use, the prognosis for patients remains poor. People with schizophrenia have an estimated life loss of nearly 30 years compared to the general population and often struggle to maintain employment, live independently or maintain meaningful interpersonal relationships.
- Schizophrenia is a complex psychiatric syndrome, defined by three major sets of symptoms: positive symptoms, also known as psychosis, negative symptoms and cognitive symptoms. Current antipsychotics only address psychosis, also known as positive symptoms, such as hallucinations and delusions, but despite treatment patients often experience residual positive symptoms throughout their lives. There are no approved treatments for the negative symptoms, such as apathy, reduced social drive and loss of motivation, or cognitive symptoms, such as changes in working memory and attention. Current approved antipsychotics treat positive symptoms and are not indicated to treat negative or cognitive symptoms of schizophrenia. Despite treatment, current antipsychotics have modest efficacy, with many patients failing to adequately respond to treatment, and are associated with burdensome side effects, such as sedation, extrapyramidal side effects such as motor rigidity, tremors and slurred speech and significant weight gain resulting in the complications of diabetes, hyperlipidemia, hypertension and cardiovascular disease. Up to 74% of patients cycle through multiple medicines within 18 months, with many failing to find an effective and/or tolerable therapy.
- An estimated 8 million people are living with dementia in the U.S., with AD as the leading cause of dementia, consisting of 60-80% of all cases. Symptoms of psychosis may present those living with dementia, including 30-50% of individuals with AD, amounting to ~3.2 million adults with AD psychosis in the U.S. Symptoms become more prevalent with increased disease severity.
- There is an unmet need for new treatments in schizophrenia that could address the positive, negative and cognitive symptoms, and are not associated with common problematic side effects associated with current dopamine-blocking therapies. There are currently no approved treatments for psychosis in Alzheimer's disease.

Milestones achieved and development status

- In November 2021, Karuna announced updates to its pipeline of novel drug candidates for the treatment of various psychiatric and neurological conditions. The clinical pipeline is led by KarXT, which is currently being evaluated in late-stage clinical trials as a potential treatment for schizophrenia and psychosis in AD.
  - **KarXT for the treatment of psychosis in adults with schizophrenia.** Karuna announced that all four Phase 3 trials in the EMERGENT program are enrolling. The program includes EMERGENT-2, a five-week inpatient trial evaluating the efficacy and safety of KarXT compared to placebo in 246 adults with schizophrenia in the U.S., EMERGENT-3, a five-week inpatient trial evaluating the efficacy and safety of KarXT compared to placebo in 246 adults with schizophrenia in the U.S. and Ukraine, EMERGENT-4, a 52-week outpatient, open-label extension trial evaluating the long-term safety and tolerability of KarXT in 350 adults with schizophrenia who completed EMERGENT-2 or EMERGENT-3, and EMERGENT-5, a 52-week outpatient, open-label trial evaluating the long-term safety and tolerability of KarXT in adults with schizophrenia who were not enrolled in EMERGENT-2 or EMERGENT-3. Karuna plans to increase the number of sites in the U.S. and Puerto Rico and allow for up to 600 patients in the trial.

1 As of March 4, 2022, PureTech's percentage ownership of Karuna was approximately 5.6% on an outstanding voting share basis. We have a right to royalty payments as a percentage of net sales from Karuna of any commercialized product covered by the granted license pursuant to a license agreement between us and Karuna.
2 The letters next to the therapeutic candidates denote whether the therapeutic candidate is a pharmaceutical product (P), biologic (B) or device (D).
3 Therapeutic candidates are investigational and have not been cleared by the FDA for use in the U.S.
4 Karuna has an active IND on file with the FDA for KarXT. Karuna also has ongoing discovery efforts to expand its pipeline. We do not control the clinical or regulatory development of Karuna's product candidates. We do not have any board designees on Karuna's board of directors, and we are not responsible for the development or commercialization of its therapeutic candidate. We have an interest in Karuna's therapeutic candidates through our equity interest as well as our right to royalty payments as a percentage of net sales of any commercialized product covered by the granted license pursuant to a license agreement between us and Karuna. Karuna is well-protected with a robust intellectual property portfolio. The disclosure above is qualified in its entirety by reference to Karuna's public filings with the SEC. Karuna was incorporated in July 2009.

Milestones achieved and development status (continued)

- **KarXT for the treatment of schizophrenia in adults who experience an inadequate response to current standard of care.** Karuna initiated the Phase 3 ARISE trial evaluating the safety and efficacy of KarXT compared to placebo as an adjunctive treatment for schizophrenia in adults who experience an inadequate response to current standard of care in November 2021. Participants in this trial will continue their currently prescribed atypical antipsychotic therapy at the same dose or regimen schedule as prior to entry in the study, and will receive a flexible dose of KarXT or placebo based on tolerability and clinical response as determined by a clinician.
- **KarXT for the treatment of psychosis in AD.** The evaluation of KarXT for the treatment of dementia-related psychosis (DRP) will initially focus on psychosis in AD, the most common subtype of DRP. The initial focus on the AD dementia subtype reflects various strategic development, regulatory and commercial considerations, and Karuna remains interested in exploring KarXT in other dementia subtypes in future development programs.
- **Discovery and early-stage pipeline.** Karuna continues to advance its earlier pipeline of muscarinic receptor-targeted programs and novel formulations of KarXT, including the initiation of a Phase 1 trial of an advanced formulation of KarXT in late 2021, as well as its artificial intelligence-based target agnostic discovery program for treating psychiatric and neurological conditions.

- In June 2021, Karuna announced data from its completed Phase 1b trial evaluating the safety and tolerability of KarXT in healthy elderly volunteers, which followed a preliminary analysis of data from the first two cohorts in the trial announced earlier in 2021. The results suggest that KarXT can be administered to elderly volunteers at doses that achieve xanomeline blood levels similar to those reported in the Phase 2 EMERGENT-1 trial in adults with schizophrenia while maintaining a favorable tolerability profile. Data from the trial also suggest that a lower dose ratio of trospium to xanomeline, compared to the ratios used in Phase 1 trials in healthy adult volunteers and in the Phase 2 EMERGENT-1 trial evaluating KarXT in adults with schizophrenia, was better tolerated by healthy elderly volunteers. The treatment-related adverse events (AEs) were similar to those observed in prior trials of KarXT, and a majority (>80%) were rated mild in severity. One serious AE of urinary retention was reported in Cohort 1. Karuna believes the report of urinary retention was related to a higher dose of trospium used in Cohort 1 compared to doses used in Cohorts 2 and 3, where urinary retention was not observed. No serious or severe AEs were observed in Cohorts 2 and 3. Consistent with prior trials of KarXT, blood pressure in healthy elderly volunteers receiving KarXT was similar to placebo, and no syncopal events were observed. Heart rate increases observed in the trial were also consistent with prior trials of KarXT.
- In November 2021, Karuna and Zai Lab (Shanghai) Co., Ltd. (Zai) announced their entry into an exclusive license agreement for the development, manufacturing and commercialization of KarXT in Greater China, including mainland China, Hong Kong, Macau and Taiwan. Under the terms of the agreement, Karuna received a $35.0 million upfront payment and is eligible to receive certain development and regulatory milestone and sales milestone payments, as well as royalties based on annual net sales of KarXT in Greater China. Zai Lab will fund substantially all development, regulatory and commercialization activities in Greater China. PureTech is also eligible to receive certain sublicense payments and royalties on sales of any commercialized product covered by the license agreement between us and Karuna pursuant to the terms of such license agreement.
- In February 2021, Karuna announced that results from the Phase 2 EMERGENT-1 trial evaluating KarXT for the treatment of schizophrenia were published in the *New England Journal of Medicine* (NEJM).
- In March 2021, Karuna completed a follow-on public offering of its common stock, from which it received net proceeds of $270.0 million.
- In November 2021, Karuna appointed Charmaine Lykins as Chief Commercial Officer. Ms. Lykins has over 25 years of psychiatry and neuroscience-focused pharmaceutical launch experience across multiple organizations recognized as leaders in developing and commercializing medicines for central nervous system disorders.

Expected milestones

- Topline data from the Phase 3 EMERGENT-2 trial is expected in mid-2022.
- Karuna plans to initiate a Phase 3 program evaluating KarXT for the treatment of psychosis in elderly patients with Alzheimer's disease in mid-2022.

Karuna's pipeline

Therapeutic Candidate[5]	Indication	Discovery/ Preclinical	Phase 1	Phase 2	Phase 3	Upcoming Milestone
KarXT	**Schizophrenia** – psychosis					EMERGENT-2 Phase 3 topline data readout mid-2022
	Schizophrenia – psychosis in adults with an inadequate response to standard of care[6]					
	Schizophrenia – negative and cognitive symptoms[7]					Phase 2 ready
	Alzheimer's disease psychosis					Phase 3 initiation mid-2022
KAR-201	**Undisclosed** – muscarinic-targeted pain candidate					
KAR-301	**Undisclosed** – muscarinic-targeted pain candidate					
KAR-401	**Undisclosed** – muscarinic-targeted pain candidate					
KAR-501	**Undisclosed** – target-agnostic drug candidate[8]					

5 Therapeutic candidates are investigational and have not been cleared by the FDA for use in the U.S.
6 Trial to evaluate KarXT when added to standard of care.
7 Planning stage.
8 In collaboration with PsychoGenics; Note – pipeline supplied by Karuna Therapeutics. Shading of bars does not conform to key used for other Founded Entity pipelines within this document.

AKILI

Founded Entity	PureTech Ownership[1]	Therapeutic Candidate[2]		Indication	Stage of Development
Akili	22.3%	EndeavorRx®[3] (AKL-T01)[4]	D[5]	Attention-deficit/hyperactivity disorder (ADHD)	Commercial
		Cognitive dysfunction in depression	D	Major depressive disorder	Proof-of-concept completed
		Cognitive dysfunction in multiple sclerosis	D	Multiple sclerosis	Proof-of-concept completed
		Attention in autism spectrum disorder	D	Autism spectrum disorder	Proof-of-concept completed
		Post-COVID cognitive dysfunction	D	Acute cognitive dysfunction	Early scientific and clinical research
		Post-ICU cognitive dysfunction	D	Acute cognitive dysfunction	Early scientific and clinical research
		Cancer-related cognitive impairment	D	Acute cognitive dysfunction	Early scientific and clinical research

- Akili is pioneering the development of game-changing technologies to usher in a new era of cognitive medicine. Focused on delivering cutting-edge digital diagnostics, treatments and monitors for cognitive impairments across disease and disorders, Akili is combining scientific and clinical rigor with the ingenuity of the technology and entertainment industries and challenging the status quo of medicine. Akili's treatments are designed to directly activate the networks in the brain responsible for cognitive function and have been rigorously tested in extensive clinical studies, including prospective randomized, controlled trials. Driven by Akili's belief that effective medicine can also be fun and engaging, Akili's products are delivered through captivating action video game experiences.
- Akili's EndeavorRx® treatment has been granted clearance by the FDA for marketing as a prescription treatment and has received a CE Mark certification in Europe as a prescription-only digital therapeutic. It is based on a patented technology that is designed to deploy sensory and motor stimuli that target and activate the neurological systems known to play a key role in certain cognitive functions, including attentional control. Akili's approach aims to improve cognitive impairment and related symptoms through improving neural processing at the functional neurological level. The treatment is delivered through an immersive video game, resulting in non-invasive, patient-friendly medicine that can be used at home.
- By combining high-quality neurological and clinical science and consumer-grade entertainment, Akili is seeking to produce a new type of medical product that can potentially offer safe, effective, scalable and personalized treatments for patients across a range of neuropsychiatric conditions and allow patients to experience medicine in a new way.
- Akili is leveraging new digital platforms for its digital therapeutic products to enable launch in a variety of models. The company is offering Akili Assist®, integrated components that enable streamlined patient service, data processing and distribution functions in its initial product launch to allow flexibility, learning and iteration as it continues to invest in the delivery of digital therapeutic solutions to the market.

Program discovery process by the PureTech team

- We were interested in identifying novel approaches to measure and improve cognition in a safe and non-invasive manner. We engaged with leading neuroscientists and clinicians who had been studying the effects of video games on cognition and the underlying neural processes accessible by sensory stimulation, and we identified and in-licensed from the University of California, San Francisco, or UCSF, the intellectual property invented by Dr. Adam Gazzaley, M.D., Ph.D., Professor of Neurology, Psychiatry and Physiology at UCSF and the inventor of the SSME platform technology, in October 2013 before his work was published as a cover story in the journal *Nature*. We then collaborated with Dr. Gazzaley to translate the underlying academic device into a medical intervention, including overseeing the initial product development and design and the implementation of the initial POC studies. We helped to build development and commercial teams and raise funds. One of the core PureTech team members who helped lead the identification and platform development is now the Chief Executive Officer of Akili.
- Akili's FDA-cleared product, EndeavorRx, is based on a patented platform technology exclusively licensed from UCSF. The proprietary platform targets cognitive interference processing while also adapting difficulty automatically in real-time, allowing individuals of wide-ranging ability levels to interact with the product in their homes without the need for physician calibration or additional hardware. Dr. Gazzaley currently serves as the Chief Scientific Advisor and a board member of Akili. Daphne Bavelier, Ph.D., Associate Professor in the Department of Brain and Cognitive Sciences at the University of Rochester and at the University of Geneva, is a co-founding scientific advisor.

Patient need and market application

- Cognitive dysfunction is a key feature of many neuropsychiatric disorders, including ADHD, ASD, MS, major depressive disorder, or MDD, mild cognitive impairment, or MCI, traumatic brain injury, or TBI, and AD. The treatment of the cognitive dysfunction associated with these conditions is only partially served, or not served at all, by currently available medications or by in-person behavioral therapy. There are approximately 6.4 million pediatric ADHD patients in the U.S. and this market – and other markets where Akili's cognitive dysfunction targeting products may address the cognitive dysfunction associated with neuropsychiatric disorders – represent significant potential opportunities for the company.
- Evidence is mounting on long-term neurological and cognitive symptoms that can persist in some COVID-19 patients after initial diagnosis, even after the virus is no longer detected in the body. A study published in *Neuropsychopharmacology* led by Drs. Abhishek Jaywant and Faith Gunning at Weill Cornell Medicine and New York-Presbyterian found that difficulties in attention, multitasking and processing speed were common in hospitalized patients recovering from COVID-19[6]. Of the patients in their study, 81% exhibited some degree of cognitive impairment[6]. Recent research also shows these cognitive impairments may persist post-hospitalization and commonly occur in "post-COVID long haulers" or "Long COVID" patients. These impairments can have a significant impact on survivors' daily functioning and quality of life, impacting the ability of most COVID-19 long haulers to work for six months or more according to a recent study[7].

Milestones achieved and development status

- In the January 2022 post-period, Akili entered into a definitive agreement to become publicly traded via a merger with Social Capital Suvretta Holdings Corp. I ("SCS") (Nasdaq: DNAA), a special purpose acquisition company. The transaction is expected to close in mid-2022, after which Akili will be listed on the Nasdaq stock market under the new ticker symbol "AKLI". The transaction implies a post-money equity value of the combined company of up to approximately $1 billion and is expected to deliver up to $412 million in gross cash proceeds to Akili, including the contribution of up to $250 million of cash held in SCS's trust account and approximately $162 million from PIPE investors at $10 per share.

1 As of December 31, 2021, PureTech's percentage ownership of Akili was approximately 22.3% on a diluted basis. This calculation includes outstanding shares, options, and warrants, but excludes unallocated shares authorized to be issued pursuant to equity incentive plans.

2 These therapeutic candidates are regulated as devices and their development has been approximately equated to phases of clinical development. With the exception of EndeavorRx, candidates are investigational and have not been cleared by the FDA for use in the U.S.

3 EndeavorRx® is a digital therapeutic indicated to improve attention function as measured by computer-based testing in children ages 8-12 years old with primarily inattentive or combined-type ADHD, who have a demonstrated attention issue. Patients who engage with EndeavorRx demonstrate improvements in a digitally assessed measure, Test of Variables of Attention (TOVA®) of sustained and selective attention and may not display benefits in typical behavioral symptoms, such as hyperactivity. EndeavorRx should be considered for use as part of a therapeutic program that may include clinician-directed therapy, medication, and/or educational programs, which further address symptoms of the disorder. There were no serious adverse events; 9.3% of subjects experienced side effects, including frustration, headache, dizziness, emotional reaction, nausea or aggression. EndeavorRx is only available to your patients through a prescription, and is not intended as a stand-alone therapeutic or a substitute for your patient's medication.

4 Multiple IRBs have determined AKL-T01 to be a non-significant risk device. Akili has obtained IRB approval independently or in collaboration with independent clinical research institutions for all past and ongoing human data collection for clinical research in the United States. We do not control the clinical or regulatory development of Akili's product candidates. We do not have a direct interest in Akili's therapeutic or therapeutic candidates. Our interest in Akili's therapeutic and therapeutic candidates is limited to our equity interest in Akili and any potential appreciation in the value of such equity interest, and we do not control the clinical or regulatory development of Akili's therapeutic candidates. Akili is well-protected with a robust intellectual property portfolio. Akili was incorporated in February 2012.

5 The letters next to the therapeutic candidates denote whether the therapeutic candidate is a pharmaceutical product (P), biologic (B) or device (D).

6 Jaywant et al. Neuropsychopharmacol. (2021).

7 David et al. Preprint. (2020).

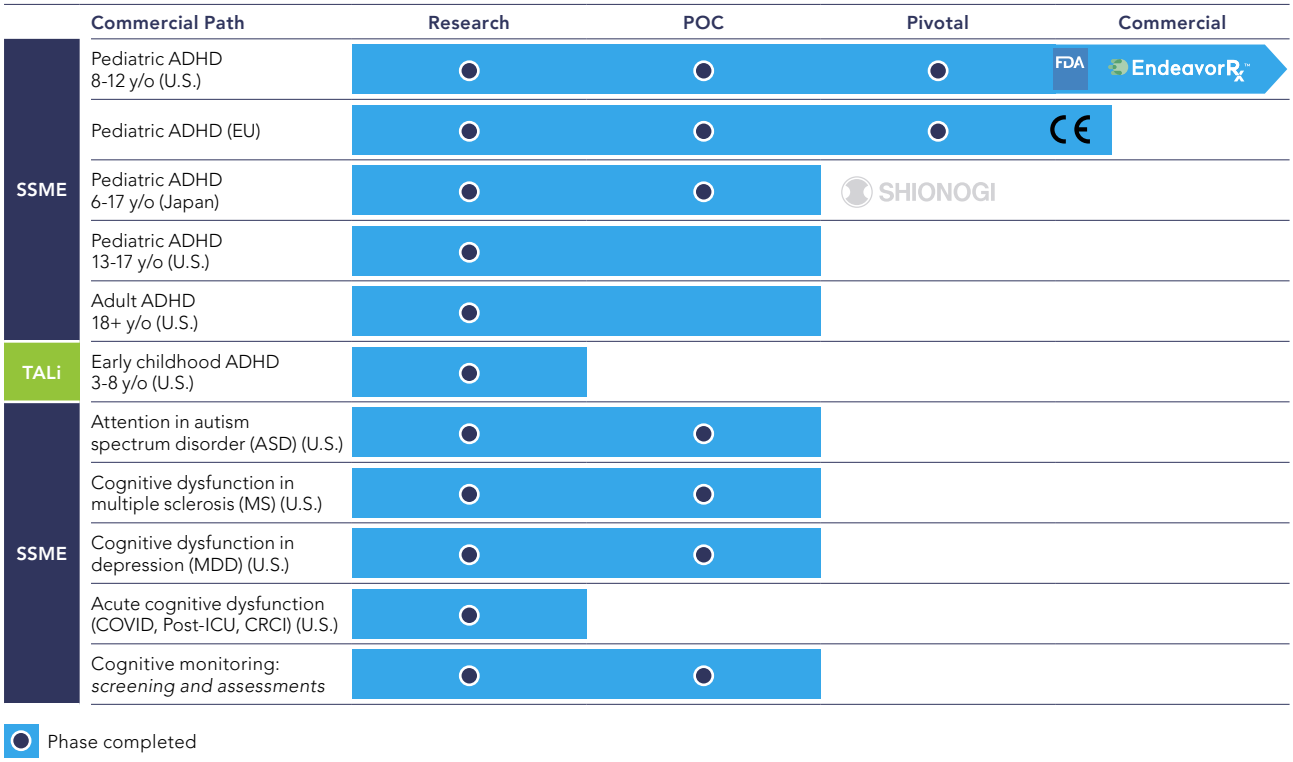
Milestones achieved and development status (continued)

- In May 2021, Akili announced the closing of a $160 million combined equity and debt financing. With the completion of the oversubscribed Series D financing, the funding is expected to accelerate commercialization of EndeavorRx, enable expansion of core technologies to treat acute and chronic cognitive disorders and drive further research and development of potential new digital therapeutics.
- In March 2021, the full data from a multi-site open-label study (the STARS Adjunct study) evaluating the impact of EndeavorRx (AKL-T01) on symptoms and functional impairments in children with ADHD was published in *Nature Digital Medicine*. Statistically significant improvement was demonstrated in all predetermined endpoints of the study, which included parent and clinician ratings of children's ADHD symptoms related impairments in daily life.
- In the February 2022 post-period, Akili announced the publication of full data in the medical journal *PLOS ONE* from a single arm, unblinded study conducted by Dr. Elysa Marco at Cortica Healthcare and Drs. Joaquin Anguera and Courtney Gallen at the University of California, San Francisco. Data from the study show that EndeavorRx treatment resulted in increased brain activity related to attention function, as measured by electroencephalography (EEG), which correlated with improvements in objective behavioral measures of attention.
- In September 2021, Akili announced topline results of a Phase 2 study of SDT-001 (Japanese version of AKL-T01). The study, conducted by Akili partner Shionogi, was designed to evaluate the feasibility, safety and efficacy of the digital therapeutic in children with ADHD and to inform the design of a potential pivotal study. To enable this clinical trial, Akili localized its AKL-T01 technology for use in the Japanese market, which included adapting for language and culture and establishing infrastructure in Japan to support the product. Results showed the treatment was well-received by patients and demonstrated improvements in ADHD inattention symptoms consistent with those seen across previous studies of AKL-T01.
- In July 2021, Akili introduced new gaming features and functionalities to its EndeavorRx treatment. Akili is releasing these new gameplay features as it expands its pre-launch activities to bring EndeavorRx to families and healthcare professionals.
- In April 2021, Akili announced collaborations with Weill Cornell Medicine, New York-Presbyterian Hospital and Vanderbilt University Medical Center to evaluate Akili digital therapeutic AKL-T01 as a treatment for patients with cognitive dysfunction following COVID-19 (also known as "COVID fog"). Under each collaboration, Akili will work with research teams at each institution to conduct two separate randomized, controlled clinical studies evaluating AKL-T01's ability to target and improve cognitive functioning in COVID-19 survivors who have exhibited a deficit in cognition.
- In August 2021, Akili and Australian digital health company TALi® (ASX: TD1), completed an agreement for Akili to license TALi's technology designed to address early childhood attention impairments. The companies plan to work together to execute clinical trials of the TALi technology in pediatric ADHD in the U.S. and pursue FDA regulatory clearance. Under the terms of the agreement, Akili will lead potential U.S. commercialization and roll-out.
- In the March 2022 post-period, Akili appointed Jon David as Chief Product Officer. A 20-year veteran of the games industry, David joins Akili to develop and execute the strategic vision of Akili's future product pipeline after serving as Vice President and General Manager at Glu Mobile, acquired in 2021 by Electronic Arts, where he led the development of both new IP and hit franchises including *Covet Fashion* and *Diner Dash Adventures*.

Expected milestones

- Akili's transaction with SCS is expected to close in mid-2022, after which Akili will be listed on the Nasdaq stock market under the new ticker symbol "AKLI".
- Akili expects to expand its pre-launch activities to bring EndeavorRx to families and healthcare professionals.
- Akili expects data from its pilot studies in COVID fog in the second half of 2022.

Akili's pipeline



Phase completed

Research: Early scientific and clinical research for the technology **POC:** Proof of Concept **Pivotal:** Pivotal study
Commercial: Product available for commercialization

GELESIS

Founded Entity	PureTech Ownership[1]	Therapeutic Candidate[2,3]		Indication	Stage of Development
Gelesis[4]	23.5%	Plenity®[5]	D	Weight management	Commercial
		Plenity® for adolescents	D	Adolescent weight management	Pending Discussion with FDA[6]
		GS200	D	Weight management in type 2 diabetes (T2D)/prediabetes	Clinical Trial Complete
		GS300	D	Non-alcoholic steatohepatitis/ non-alcoholic fatty liver disease (NASH/NAFLD)	Clinical
		GS500	D	Functional constipation	Pivotal

- Gelesis is developing a novel category of therapies for obesity and GI-related chronic diseases. In April 2019, Gelesis received clearance from the FDA for its first product, Plenity (Gelesis100), an aid for weight management in adults with excess weight or obesity, a BMI of 25-40 kg/m^2, when used in conjunction with diet and exercise. In June 2020, Gelesis received a CE Mark for Plenity as a class III medical device indicated for weight loss adults with a BMI of 25-40 kg/m^2, when used in conjunction with diet and exercise, which allows Gelesis to market Plenity throughout the European Economic Area and in other countries that recognize the CE Mark.
- Given challenges associated with pharmacological and invasive surgical treatments for obesity, Gelesis designed an approach with an oral, non-invasive, non-systemic mechanism of action and a highly favorable safety and efficacy profile. Gelesis' therapeutic candidates work in the GI tract and pass through the body without being absorbed. Their superabsorbent hydrogels mimic some of the properties of raw vegetables. They are conveniently administered in capsules and act locally in the stomach and intestines, helping people feel satisfied with smaller portions so they can eat less and lose weight, while still enjoying foods they love as part of a reduced-calorie diet. Because Gelesis' technology acts mechanically and is not systemically absorbed, the therapeutic candidates are treated as devices for regulatory approval purposes.

Program discovery process by the PureTech team

- We were interested in creating an effective and safe therapy for obesity given the tremendous need, significant health implications and failure of prior approaches to effectively engage and serve the breadth of the population affected. We consulted with leading obesity experts to brainstorm the characteristics of an ideal approach, which we decided was an orally administered mechanically acting device that's expected to have a favorable safety and tolerability profile, and we then conducted a worldwide search for compelling technologies meeting these criteria. We identified and in-licensed the core intellectual property from one of our academic collaborators in October 2008, and we subsequently co-invented additional intellectual property around a novel class of biocompatible, superabsorbent hydrogels. One of the core PureTech team members involved in the initial identification and development process subsequently assumed the role of Chief Executive Officer of Gelesis, and successfully attracted financing and built a strong development and commercial leadership team.

- The Gelesis advisory team is comprised of leading experts in obesity and its related comorbidities, clinical research and development and advanced biomaterials, including Caroline Apovian, M.D., Professor of Medicine and Pediatrics, Boston University School of Medicine and Co-Director, Center for Weight Management and Wellness, Endocrinology, Diabetes and Hypertension, Brigham and Women's Hospital; Louis J Aronne, M.D., FACP, Director of the Comprehensive Weight Control Program at Weill Cornell Medicine; Arne Astrup, M.D., Head of Department of Nutrition, Exercise and Sports at University of Copenhagen; Ken Fujioka, M.D., Director of the Nutrition and Metabolic Research Center and the Center for Weight Management at the Scripps Clinic; James Hill, Ph.D., Chairman, Department of Nutrition Sciences, Director, Nutrition Obesity Research Center, University of Alabama; Professor of Medicine and Pediatrics, University of Colorado; Scott Kahan, M.D., MPH, Director of the National Center for Weight and Wellness; Lee M Kaplan, M.D., Ph.D., Director of the Obesity, Metabolism and Nutrition Institute at Massachusetts General Hospital; Bennett Shapiro, M.D., Co-Founder and Non-Executive Director at PureTech and former Executive Vice President of Research for Merck; and Angelo Tremblay, Ph.D., Professor at Laval University.

Patient need and market application

- Excess weight is growing rapidly in prevalence worldwide, with approximately 70% of American adults struggling with overweight and obesity. Globally, there are more than 1.9 billion adults 18 years of age or older who have overweight and 600 million who have obesity. In addition to the adult population, the pediatric population is also suffering from an obesity epidemic. According to the CDC, by 2016, obesity in the U.S. has more than tripled in children and adolescents since the 1970s. In 2017-2018, more than one-third of children and adolescents had excess weight or obesity. According to a study by WHO, in 2016, over 340 million children and adolescents aged 5-19 had excess weight or obesity. Obesity-related conditions, such as heart disease, stroke, type 2 diabetes, NASH/NAFLD and certain types of cancer, are some of the leading causes of preventable death. Functional constipation and NASH/NAFLD affect approximately 30 million and 80 to 100 million individuals, respectively, in the U.S. Type 2 diabetes and prediabetes affect approximately 32 million and 88 million individuals, respectively, in the U.S.
- Current treatments for patients with overweight and obesity begin with lifestyle modification, such as diet and exercise. When healthy eating and physical activity fail to produce the desired results, physicians may consider pharmaceutical therapies, device implantation or surgical treatments, such as gastric bypass and gastric banding (for patients with more severe obesity). These approaches are associated with significant safety concerns, lifestyle impact, complexity of use, high cost and compliance issues that have limited their adoption.
- Plenity, indicated for adults with a BMI of 25-40 kg/m^2 when used in conjunction with diet and exercise, thus giving it the broadest label of any prescription weight management approach, has an important market segment for this product which is adults with BMI <35 kg/m^2 (approximately 130 million adults in the U.S.). The consumer expectations of weight loss within this group and the desire for a strong safety profile provide a particularly differentiated opportunity for Plenity.

1 As of March 31, 2022, PureTech's beneficial ownership of Gelesis was approximately 23.5%. PureTech is eligible to receive additional earnout shares in accordance with the terms of the business combination agreement. PureTech is also eligible to receive certain payments from Gelesis under its license agreement, including sublicense payments and royalties on sales of certain products, including Plenity.

2 The letters next to the therapeutic candidates denote whether the therapeutic candidate is a pharmaceutical product (P), biologic (B) or device (D).

3 These therapeutic candidates are regulated as devices and their development has been approximately equated to phases of clinical development. With the exception of Plenity, therapeutic candidates are investigational and have not been cleared by regulatory authorities for use in any jurisdiction.

4 Gelesis' completed and ongoing studies have been approved by the applicable reviewing Institutional Review Boards, or IRBs, as nonsignificant risk device studies. Gelesis also has ongoing discovery efforts to expand its pipeline. Our board designees represent a minority of the members of the board of directors of Gelesis, and we do not control the clinical or regulatory development or commercialization of Gelesis' therapeutics and therapeutic candidates. We have an interest in Gelesis' therapeutic candidates through our minority equity investment as well as our right to royalty payments as a percentage of net sales pursuant to a license agreement between us and Gelesis. Gelesis is well protected with a robust intellectual property portfolio. Gelesis was incorporated in February 2006.

5 Important Safety Information about Plenity®: Patients who are pregnant or are allergic to cellulose, citric acid, sodium stearyl fumarate, gelatin, or titanium dioxide should not take Plenity. To avoid impact on the absorption of medications: For all medications that should be taken with food, take them after starting a meal. For all medications that should be taken without food (on an empty stomach), continue taking on an empty stomach or as recommended by your physician. The overall incidence of side effects with Plenity was no different than placebo. The most common side effects were diarrhea, distended abdomen, infrequent bowel movements, and flatulence. Contact a doctor right away if problems occur. If you have a severe allergic reaction, severe stomach pain, or severe diarrhea, stop using Plenity until you can speak to your doctor. Rx Only. For the safe and proper use of Plenity or more information, talk to a healthcare professional, read the Patient Instructions for Use, or call 1-844-PLENITY.

6 Contingent on FDA review of the research plan.

Milestones achieved and development status

- In December 2021, Gelesis announced that Plenity is now broadly available across the U.S. to adults who meet the prescription criteria.
- In the January 2022 post-period, Gelesis announced the completion of its business combination with Capstar Special Purpose Acquisition Corp. (NYSE: CPSR) ("Capstar") to become Gelesis Holdings, Inc. The company began trading on the New York Stock Exchange under the ticker symbol "GLS" on January 14, 2022.
- In the January 2022 post-period, Gelesis launched the "Who Said?" marketing campaign across the U.S., which challenges many long-held cultural and societal assumptions around weight loss. Plenity's multichannel campaign encompasses TV, digital, social and Out of Home (OOH) to grow awareness of Plenity's novel approach to weight management.
- In the March 2022 post-period, Gelesis announced preliminary results from its broad awareness media campaign, noting that within the first three weeks, Gelesis saw a 3-fold increase in web traffic and 3.5-fold increase in the number of individuals seeking a new prescription compared to previous months when supply was limited.
- In November 2021, Gelesis' first commercial-scale manufacturing line was completed and validated, and the company received a $30 million fully paid pre-order, in addition to the $10 million pre-order received in January 2021, for Plenity from its partner Ro, a leading U.S. direct-to-patient healthcare company.
- In late 2021, Gelesis completed a preliminary analysis of the LIGHT-UP study, a multicenter, randomized, double-blind, placebo-controlled, investigational study that enrolled 254 subjects with overweight or obesity who also have prediabetes or type 2 diabetes, and that analysis remains underway. The study was designed to assess the change in body weight in adults after six months of treatment with a new oral superabsorbent hydrogel (GS200) or placebo. The study met both of its primary endpoints: the proportion of participants who achieved at least 5% body weight loss (defined as "Responders") and the change in body weight as compared to placebo after six months of therapy. The LIGHT-UP study was conducted at 36 clinical sites in Europe and North America with 208 subjects who completed the 6-month study.
- In November 2021, Gelesis announced a publication in Nature's *Scientific Reports* describing the genesis of the underlying technology and engineering process for Gelesis' non-systemic superabsorbent hydrogels. The paper describes their therapeutic approach for weight management as well as possible future solutions for other gut-related conditions.
- In May 2021, Gelesis presented a scientific poster at the American Association of Clinical Endocrinology (AACE) 2021 Annual Virtual Meeting. The post-hoc analysis showed that treatment for weight management with Plenity decreased a marker for liver fibrosis (the NAFLD fibrosis score) compared to placebo.
- In the January 2022 post-period, Gelesis announced the appointment of Inogen Co-Founder and Former CFO, Ali Bauerlein, to its Board of Directors and Audit Committee. Ms. Bauerlein brings success in scaling to $300M+ revenue in direct-to-consumer business model and public company execution as Gelesis plans to scale Plenity to meet growing consumer demand.
- In April 2021, Gelesis announced the appointment of marketing executive Jane Wildman to its Board of Directors. Ms. Wildman has extensive experience as a board member, President and Chief Marketing Officer across Fortune-25, mid-sized and start-up companies, including over 25 years at Procter & Gamble.
- In December 2021, Gelesis announced the appointment of leading health and nutrition authority Joy Bauer, MS, RDWN, CDN as Chief Nutrition Officer of Plenity.

Gelesis' pipeline

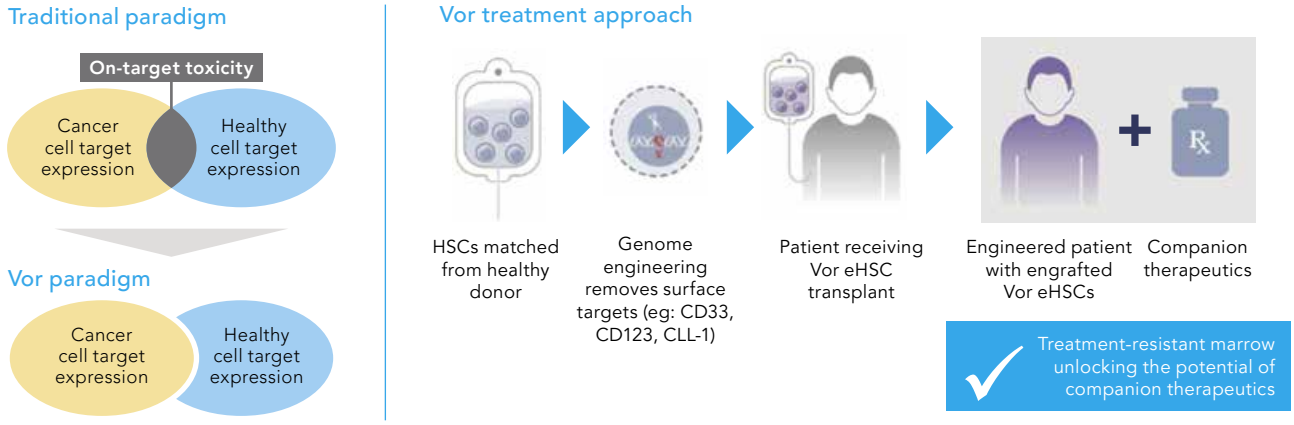
Product	Research Focus	Preclinical	Clinical	Pivotal	Clearance
Plenity	Weight Management in Patients with Excess Weight and Obesity	Completed	FLOW completed	GLOW completed	FDA Cleared & EU CE Mark
Plenity® for adolescents*	Weight Management in Adolescent Patients with Excess Weight and Obesity				
GS200*	Weight Management and Glycemic Control in Patients with Type 2 Diabetes and Pre-diabetes		LIGHT-UP Complete, Primary Endpoints Achieved		
GS300*	NAFLD/NASH	Ongoing			
GS500*	Functional Constipation (formerly classified as CIC)		Pilot Clinical Study Completed		

* Products are investigational and have not been cleared by the FDA for use in the U.S.

Founded Entity	PureTech Ownership[1]	Therapeutic Candidate[2,3]		Indication	Stage of Development
Vor Bio[4]	8.6%	VOR33 (CD33)	B	Acute myeloid leukemia Myelodysplastic syndromes, myeloproliferative neoplasms	Phase 1/2a Preclinical
		VCAR33[5]	B	Bridge-to-transplant AML	Phase 1/2

- Vor Bio is a clinical-stage cell and genome engineering company that aims to change the standard of care for patients with blood cancers by engineering hematopoietic stem cells (HSC) to enable targeted therapies post-transplant. The only way for many of these patients to achieve durable remission or a cure is through hematopoietic stem cell transplant, or HSCT. Despite this, approximately 40% of AML patients relapse within two years of their transplant and face an extremely poor prognosis, with a two-year survival rate of less than 20%. Though targeted therapies are an effective treatment for many patients in transplant settings who relapse, these therapies are limited by toxicities resulting from the expression of the surface targets on healthy cells, including these new transplanted cells, which is referred to as on-target toxicity.

Changing the traditional tumor target paradigm



- Vor Bio's proprietary platform leverages its expertise in HSC biology and genome engineering to remove surface targets expressed by cancer cells by genetically modifying HSCs. By removing these targets, Vor Bio makes these HSCs and their progeny treatment-resistant to targeted therapies and enables these treatments to selectively destroy cancerous cells while sparing healthy cells. As a result, Vor Bio's engineered HSCs (eHSC) are designed to limit the on-target toxicities associated with these targeted therapies, or companion therapeutics, thereby enhancing their utility and broadening their applicability.
- Vor Bio's platform and expertise allow it to advance its goal of replacing standard HSC transplants with next-generation, treatment-resistant eHSCs that unlock the potential of highly potent targeted therapies.

Program discovery process by the PureTech team

- We were interested in approaches to treat hematological malignancies that currently have poor response rates or poor adverse event profiles despite recent advances in cell therapies and targeted therapies. We engaged leading hematological cancer specialists and we became aware of work from the laboratory of Vor Bio Scientific Board Chair, Siddhartha Mukherjee, M.D., Ph.D., Assistant Professor of Medicine at Columbia University and Pulitzer Prize-winning author of *The Emperor of All Maladies: A Biography of Cancer*. Dr. Mukherjee pioneered the idea of genetically engineering stem cells to eliminate a particular target such that healthy stem cells and progeny cells would be spared from targeted cancer therapy. We worked with Dr. Mukherjee on this intellectual property, which Vor Bio exclusively in-licensed from Columbia in April 2016, and on advancing this concept through critical POC experiments. With our support, Vor Bio secured additional intellectual property rights (both in-licensed from Columbia and owned by Vor Bio), assembled an excellent research team and completed a round of fundraising.

Patient need and market application

- The prognosis for relapsed and refractory blood-borne malignancies is very poor and can be measured in a few months, depending on patient-specific risk factors. There are an estimated 42,500 new diagnoses of AML each year in the U.S., Europe and Japan. The two-year survival rate for patients with AML who relapse post-transplant is less than 20%, but there are significant differences in prognosis depending on several factors, including the age of the patient at diagnosis.
- Targeted therapies, such as CAR-T cells and bispecific antibodies, antibody-drug conjugates and conventional mAbs, have shown clinical activity, particularly in patients with certain hematologic malignancies expressing B cell markers. However, these targeted therapies frequently target both cancer and normal cells, causing substantial toxicities and limiting their potential. There is a need for new strategies that can enable selectively targeting cancer cells with limited impact on a patient's normal cells.

Milestones achieved and development status

- In February 2021, Vor Bio announced the pricing of its initial public offering of common stock on the Nasdaq Global Market under the symbol "VOR". The aggregate gross proceeds to Vor Bio from the offering were approximately $203.4 million, before deducting the underwriting discounts and commissions and other offering expenses payable by Vor Bio.
- In the March 2022 post-period, Vor Bio announced VCAR33 is now made up of two programs with different cell sources. The VCAR33 programs are chimeric antigen receptor T (CAR-T) cell therapy candidates designed to target CD33, a clinically-validated target for AML.
  - VCAR33^{AUTO} uses autologous cells from each patient, and is being studied in an ongoing Phase 1/2 clinical trial sponsored by the National Marrow Donor Program (NMDP) in young adult and pediatric patients with relapsed/refractory AML in a bridge-to-transplant study.
  - VCAR33^{ALLO} uses allogeneic healthy donor-derived cells. There has been an increasing appreciation for the value of cell phenotype in CAR-T approaches, and HLA-matched healthy donor cells are a potentially superior cell phenotype with improved persistence and in vivo expansion capability.

1 As of March 4, 2022, PureTech's ownership percentage of Vor Bio was approximately 8.6% on an outstanding voting share basis. This calculation includes outstanding shares, options, and warrants, but excludes unallocated shares authorized to be issued pursuant to equity incentive plans.
2 The letters next to the therapeutic candidates denote whether the therapeutic candidate is a pharmaceutical product (P), biologic (B) or device (D).
3 Therapeutic candidates are investigational and have not been cleared by regulatory authorities for use in any jurisdiction.
4 Vor Bio has an active IND on file with the FDA for VOR33 and an active IND is on file for VCAR33. PureTech does not have a direct interest in Vor Bio's therapeutic candidates or its proprietary platform. PureTech's interest in Vor Bio's therapeutic candidates and proprietary platforms is limited to its non-controlling equity interest in Vor Bio and any potential appreciation in the value of such equity interest and PureTech does not control the clinical or regulatory development of Vor Bio's therapeutic candidates. Vor Bio is well-protected with a robust intellectual property portfolio. Vor Bio was incorporated in December 2015.
5 The VCAR33 construct is being studied in a Phase 1/2 clinical trial sponsored by the National Marrow Donor Program ("NMDP"), and the timing of data release is dependent on the investigators conducting the trial.

Milestones achieved and development status (continued)

- In the March 2022 post-period, Vor Bio announced it plans to collect initial data on VOR33 from the VBP101 clinical trial and initial clinical data from the VCAR33^{ALLO} program prior to IND submission for the Treatment System following ongoing discussions with the FDA and alongside improved scientific understanding of the differences in T-cell sources. The combination of VOR33 followed by treatment with VCAR33^{ALLO} in the post-transplant setting may transform patient outcomes and offer the potential for cures for patients that have limited treatment options. The VOR33 + VCAR33 Treatment System utilizes the same healthy donor allogeneic cell source for both VOR33 and VCAR33^{ALLO}. Vor Bio believes this approach will be a superior development pathway for this novel-novel treatment combination.
- In September 2021, Vor Bio announced that the FDA granted Fast Track designation to VOR33 for the treatment of AML, allowing for potential facilitated development and expedited review process.
- In September 2021, Vor Bio announced it is actively enrolling VBP101, a Phase 1/2a clinical trial for AML patients who currently have limited treatment options. Vor Bio intends to investigate the VOR33/VCAR33 Treatment System, entailing VOR33 eHSC therapy followed by VCAR33 as a companion therapeutic, initially for transplant-eligible patients suffering from AML. Vor Bio believes VCAR33 could be a potent anticancer therapy that, when combined with VOR33, could help obviate severe on-target myeloablative toxicities and unlock the efficacy potential of VCAR33.
- In November 2021, Vor Bio announced its first multi-targeted Treatment System comprising VOR33-CLL1 multiplex-edited eHSC therapy and VCAR33-CLL1 multi-specific CAR-T therapy. Vor continues to make progress on editing multiple antigens with its eHSC platform. Vor Bio's research demonstrates that multiplex genome editing of allogeneic hematopoietic stem cells may represent another existing strategy to efficiently and safely edit multiple genes in blood stem cells, allowing the potential use of multi-targeted blood cancer therapies.
- In June 2021, Vor Bio announced the build-out of an in-house clinical manufacturing facility in Cambridge, Massachusetts in the same premises as Vor Bio's current headquarters, to support flexible manufacturing for the company's eHSC and CAR-T product candidate pipeline for patients with blood cancers. Vor Bio anticipates that the facility will be operational in 2022.
- In July 2021, Vor Bio announced the formation of a collaboration with Janssen Biotech, Inc., one of the Janssen Pharmaceutical Companies of Johnson & Johnson, to develop eHSC transplants combined with bi-specific antibody therapy for AML. The agreement was facilitated by Johnson & Johnson Innovation. Under the terms of the collaboration, Vor Bio will investigate the combination of these two technologies into a treatment solution, pairing Vor's "invisible" eHSC transplant platform with one of Janssen's bi-specific antibodies in development for AML. The collaboration agreement provides that each company retains all rights and ownership to their respective programs and platforms.
- In June 2021, Vor Bio entered into a multi-year strategic collaboration and license agreement with Abound Bio to research both single-and-multi-targeted CAR-T treatments to be used in combination with Vor's eHSC platform, with the goal of generating novel treatment systems for patients fighting AML and other devastating forms of blood cancer.
- In January 2021, Vor Bio announced that the FDA had accepted the company's IND application for VOR33. In May 2021, Vor Bio announced that it received the Canadian clinical trial application clearance for VOR33 from Health Canada.
- Leveraging its proprietary platform, Vor Bio is exploring additional surface targets such as CD123, EMR2 and CD5, including multiplex genome engineering approaches where multiple surface targets are removed. Additionally, Vor Bio is conducting ongoing discovery efforts in commonly transplanted hematologic malignancies. PureTech does not control the clinical or regulatory development of Vor Bio's therapeutic candidates.
- In June 2021, Vor Bio announced the appointment of Matthew R. Patterson as Chairman of its Board of Directors. Mr. Patterson brings nearly 30 years of senior leadership experience in the research, development and commercialization of innovative therapeutics, most recently at Audentes Therapeutics, Inc., which he co-founded and led as the company's Chief Executive Officer from its inception in 2012 through its acquisition by Astellas Pharma Inc. in January 2020.

Expected milestones

- Vor Bio expects to report initial clinical data from VBP101, a Phase 1/2a clinical trial for VOR33 for patients with AML, in the second half of 2022.
- Data from the ongoing Phase 1/2 NMDP-sponsored clinical trial evaluating VCAR33^{AUTO} in young adult and pediatric patients with relapsed/refractory AML in a bridge-to-transplant study are expected in 2022, depending on investigator's timing of data release.[5]
- Vor Bio plans to submit an IND application in the first half of 2023 to support a Phase 1/2 clinical trial of VCAR33^{ALLO} for patients with relapsed/refractory AML.
- Vor Bio anticipates its in-house clinical manufacturing facility in Cambridge, MA will be operational in 2022.
- Vor Bio plans to collect initial data on VOR33 from the VBP101 clinical trial and initial clinical data from the VCAR33^{ALLO} program prior to IND submission for the VOR33 + VCAR33 Treatment System.
- Vor Bio plans to share preclinical data on its VOR33-CLL1 + VCAR33-CLL1 Treatment System approach at upcoming scientific meetings in 2022.
- Leveraging its proprietary platform, Vor is exploring additional surface targets such as CD123, EMR2 and CD5 including multiplex genome engineering approaches where multiple surface targets are removed.
- Vor Bio is conducting ongoing discovery efforts in commonly transplanted hematologic malignancies.

Vor Bio's pipeline

Therapeutic Candidate	Indication	Discovery/ Preclinical	Phase 1	Phase 2	Phase 3	Upcoming Milestone
VOR33 (CD33)	Acute myeloid leukemia					Phase 1/2a topline data readout 2H 2022
	Myelodysplastic syndromes, myeloproliferative neoplasms					
VCAR33	Bridge-to-transplant AML					Phase 1 data readout 2022
VOR33/VCAR33 (Treatment System)	Acute myeloid leukemia					IND filing 2H 2022 following initial VOR33 and NMDR clinical data[6]
VOR33-CLL1 + VCAR33-CLL1 (Treatment System)	Acute myeloid leukemia					

Phase in progress Phase completed

VEDANTA BIOSCIENCES

Founded Entity	PureTech Ownership[1]	Therapeutic Candidate[2,3]		Indication	Stage of Development
Vedanta[4]	41.4%	VE303	B	*C. difficile*	Phase 3 Ready
		VE202	B	Inflammatory bowel disease	Phase 2 Ready
		VE416	B	Food allergy	Phase 1/2
		VE800	B	Solid tumors	Phase 1
		VE707	B	Gram-negative infections	Preclinical

- Vedanta is developing a new category of oral therapies based on defined consortia of bacteria isolated from the human microbiome and grown from pure clonal banks. The human microbiome is increasingly implicated in various immune-mediated diseases. Vedanta is a leader in the field with capabilities and deep expertise to discover, develop and manufacture live bacteria drugs. These include what is believed to be a leading intellectual property position with the largest collection of human microbiome-associated bacterial strains, a suite of proprietary assays to select pharmacologically potent strains, vast proprietary datasets from human interventional studies and facilities for current good manufacturing practice, or CGMP, compliant manufacturing of rationally defined bacterial consortia in powder form. All of this work has helped move the microbiome field beyond correlation to causation, and beyond fecal transplants or fractions to defined, characterized biologic drugs.

Rationally defined bacterial consortia

Oral administration in capsule form

Bacterial consortia are easily administered in lyophilized **oral** capsule form.

Colonization of the intestine

The active ingredients travel down the GI tract and **colonize** the intestine.

They shift the gut microbiota composition and **provide colonization resistance** against gut pathogens.

Stimulation of targeted immune responses

They **elicit a range of immune responses** – immunoregulatory and immunopotentiating.

Program discovery process by the PureTech team

- We were interested in translating the crosstalk between the immune system and commensal microbes that live in our bodies into therapeutics to modulate a range of immunological processes. We engaged with leading world-renowned experts in immunology, including Dr. Ruslan Medzhitov, Professor of Immunobiology at Yale; Dr. Alexander Rudensky, a tri-institutional Professor at the Memorial Sloan-Kettering Institute, the Rockefeller University, and Cornell University; Dr. Dan Littman, Professor of Molecular Immunology at NYU; Dr. Brett Finlay, Professor at the University of British Columbia; and Dr. Kenya Honda, Professor at the School of Medicine, Keio University. Drs. Honda and Rudensky demonstrated the role of the microbiota in inducing regulatory T cells and uncovered some of the molecular mediators, known as short-chain fatty acids.
- We identified and in-licensed intellectual property from Dr. Honda when he was at Tokyo University in November 2011, before his seminal work was published in the journals *Science* and *Nature*. Based on Dr. Honda's work, we pioneered the concept of defined consortia of microbes to modulate the immune system or treat bacterial infections. We played a critical role in the initial product development, initial experiments and planning of key clinical studies, business development and fundraising, and a core PureTech team member who helped lead the identification and platform development is now the Chief Executive Officer of Vedanta.

Patient need and market potential

- *Clostridioides difficile* infection (CDI): The Centers for Disease Control and Prevention considers CDI one of the most urgent bacterial threats. *C. difficile* infections account for approximately 12,800 deaths each year in the U.S. alone and there are approximately 500,000 cases annually, of which approximately 100,000 patients experience recurrence. Existing interventions include antibiotics such as vancomycin, fidaxomicin, or metronidazole, which have the undesirable side effect of damaging the gut microbiome and leaving patients vulnerable to re-infection. An alternative intervention, fecal microbiota transplantation (FMT), is an experimental procedure that is exceedingly difficult to standardize and scale and is fraught with potential safety issues.
- Inflammatory Bowel Disease (IBD): Ulcerative colitis and Crohn's disease, the most common types of IBD, affect about one million adults in the U.S. and about seven million globally and the prevalence of IBD is expected to continue to grow. Many of the existing interventions are limited by toxicities and systemic immune suppression.
- Allergies: Food allergies are a growing U.S. public health concern and have an estimated annual economic cost near $25 billion. Peanut allergies specifically affect an estimated 4.6 million adults in the U.S. Current treatment options primarily center around allergen avoidance. Desensitization regimens in development have limited efficacy, are risky, require treatment for life and may not be cost-effective. Vedanta's therapeutic candidate, VE416, is being developed to safely induce permanent tolerance to food allergens including peanuts.
- Immuno-Oncology: Despite profound survival improvements in some patients, immune checkpoint inhibitors targeting PD-1, PDL-1 and CTLA-4 are only effective in 20-30% of patients. Common tumor types for which checkpoint inhibitors are utilized include lung, bladder, skin and renal cancers. Vedanta's immuno-oncology therapeutic candidate, VE800, is designed to act in combination with approved checkpoint inhibitors and potentially other immunotherapies to safely improve their efficacy.
- The Microbiome Field: Moving Beyond FMTs and Fractions
  - Unlike FMTs, which require the use of donors and are untargeted, inherently variable procedures, Vedanta's approach is based on bacterial consortia therapeutics, which are defined drug compositions produced from clonally isolated bacteria that can trigger targeted immune responses.
  - Unlike single-strain probiotics, defined consortia can robustly shift the composition of the gut microbiota and provide colonization resistance against a range of intestinal infectious pathogens.
  - Vedanta's novel therapeutic candidates are administered as a lyophilized powder in a capsule dosage form, designed to have specific effects on the immune system, including restoring the balance of the microbiome in the gut to treat immune and infectious diseases and immunopotentiating responses to treat cancer.

1 As of December 31, 2021, PureTech's percentage ownership of Vedanta Biosciences was approximately 41.4% on a diluted basis. This calculation includes outstanding shares, options, and warrants, but excludes unallocated shares authorized to be issued pursuant to equity incentive plans.
2 The letters next to the therapeutic candidates denote whether the therapeutic candidate is a pharmaceutical product (P), biologic (B) or device (D).
3 Therapeutic candidates are investigational and have not been cleared by regulatory authorities for use in any jurisdiction.
4 Active INDs or the foreign regulatory equivalent are on file for VE202, VE303, VE416 and VE800. Our board designees represent a majority of the members of the board of directors of Vedanta, but Vedanta has its own independent management team. Our role in the development of Vedanta's therapeutic candidates is through our representation on its board of directors and our role as a substantial shareholder. Vedanta intellectual property portfolio is believed to provide a dominant position for the development and commercialization of microbiome medicines based on defined consortia of gut bacteria. Vedanta was incorporated in December 2010.
5 Nearly 100,000 isolates obtained from >275 healthy donors from 4 continents, >3,000 WGS, extensively phenotyped.

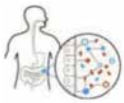
Milestones achieved and development status

- In October 2021, Vedanta announced that its Phase 2 clinical trial of VE303, an orally administered investigational live biotherapeutic product (LBP) in development for the prevention of recurrent CDI in high-risk patients, met its primary endpoint of preventing disease recurrence through Week 8. VE303 achieved a 31.7% absolute risk reduction in rate of recurrence when compared with placebo, representing a greater than 80% reduction in the odds of a recurrence. This is believed to be the most advanced clinical trial of an investigational drug based on a rationally defined bacterial consortium, a microbiome-based therapeutic approach that delivers orally administered candidates of precisely known composition that can be manufactured with pharmaceutical-grade consistency. Based on the Phase 2 data, the Biomedical Advanced Research and Development Authority (BARDA) exercised its first contract option for additional funding of $23.8 million, pursuant to its existing 2020 contract with Vedanta, to support a planned Phase 3 clinical trial of VE303.
- In January 2021, Vedanta announced a $25 million investment from Pfizer, as part of the Pfizer Breakthrough Growth Initiative. Vedanta will retain control of all of its programs and has granted Pfizer a right of first negotiation on VE202. As part of the investment, Michael Vincent, M.D., Ph.D., Senior Vice President and Chief Scientific Officer, Inflammation & Immunology Research Unit at Pfizer, joined Vedanta's Scientific Advisory Board.
- In July 2021, Vedanta closed a $68 million financing, which included the $25 million investment from Pfizer announced in January 2021.
- In late 2021, Vedanta completed the build-out of its Phase 3 and commercial launch CGMP manufacturing facility for supply of VE303.
- A Phase 1/2, investigator-sponsored clinical study exploring use of VE416 in combination with an oral peanut immunotherapy is underway at Massachusetts General Hospital. VE416 consists of seven bacterial strains of the Clostridia class, which were selected based on their ability to induce immune tolerance in the gut.
- A new Phase 2 investigator-sponsored trial evaluating VE303 in patients with hepatic encephalopathy (HE) was initiated by the University of Michigan Hospitals-Michigan Medicine. This randomized, double-blind, placebo-controlled trial is planned to enroll up to 18 adult patients with a confirmed diagnosis of cirrhosis and history of at least one episode of overt HE.
- In July 2021, Vedanta announced results from the Phase 1 study evaluating the safety and initial clinical activity of VE800, and immuno-oncology therapeutic candidate, in combination with Bristol Myers Squibb's Opdivo® (nivolumab) in 54 patients across select types of advanced or metastatic cancers. VE800 demonstrated an acceptable safety and tolerability profile, although the observed response rates did not meet the prespecified criteria to expand into the next stage of the study. Vedanta is analyzing blood, stool, and tumor samples from patients in whom response or disease control was observed in order to profile patient subtypes that might benefit from microbiome manipulation. Vedanta plans to present the results at a future medical conference and will continue work to identify cancer settings and patient populations that might benefit from microbiome manipulation with its defined bacterial consortia.
- In February 2021, Vedanta announced the appointment of Mark Mullikin as Chief Financial Officer. Mr. Mullikin brings 25 years of experience raising and deploying capital for life sciences companies, and most recently held leadership roles in finance and investor relations at publicly traded Editas Medicine and Novartis.
- In October 2021, Vedanta announced the appointment of Simona Levi as Chief Legal Officer and Corporate Secretary. Dr. Levi brings over 25 years of U.S. and international legal experience with private and public companies across the life sciences industry, focusing on complex transactions, intellectual property law and litigation and corporate governance.
- Vedanta also has ongoing discovery efforts to expand its pipeline, including VE707. VE707 is Vedanta's preclinical discovery program for the prevention of infection and recurrence of colonization with several multidrug-resistant organisms, including carbapenem-resistant Enterobacteriaceae and extended-spectrum beta lactamase producers, which are leading causes of the most common hospital-acquired infections.

Expected milestones

- Vedanta plans to initiate a Phase 3 clinical trial of VE303 in patients at high risk for recurrent CDI.
- Vedanta plans to initiate a Phase 2 trial of VE202 in patients with mild to moderate ulcerative colitis.

From correlation to causation: field-leading platform for development of microbiome drugs



1

Interrogate human interventional data to generate hypothesis on which bacteria **correlate with clinical response**

2

Establish microbiome **role in driving physiological response** *in vivo*, identify key taxa responsible

3

Screen what is believed to be the world's largest microbiome library[5] in proprietary assays to select strains with desired pharmacology

4

Assemble, optimize **customized consortia** using computational tools, co-culture systems and animal model testing

5

Manufacture CGMP-grade drug supplies at in-house, state-of-the-art facility

6

Test defined consortia in humans to **establish engraftment, safety and efficacy**

Correlation ▸ ▸ ▸ **Role of bacterial strains in disease pathology** ▸ ▸ ▸ **Causation**

Vedanta's pipeline

Therapeutic Candidate[3]	Indication	Funding	MOA	Discovery/ Preclinical	CMC	Phase 1	Phase 2	Phase 3
VE303	*C. difficile*	CARB-X						
VE202	Inflammatory bowel disease							
VE800	Solid tumors in combination with nivolumab *(Opdivo)*							
VE707	Gram-negative infections	CARB-X						
Investigator Sponsored Trials	**VE303** Hepatic Encephalopathy							
	VE416 Food Allergy in combination with oral immunotherapy							

Phase in progress Phase completed

follica

Founded Entity	PureTech Ownership[1]	Therapeutic Candidate[2]		Indication	Stage of Development
Follica[3]	76.0%	FOL-004	P/D[4]	Androgenetic alopecia	Phase 3 Ready

- Follica is developing a regenerative biology platform designed to treat androgenetic alopecia, epithelial aging and other related indications. Follica's approach is based on generating the "embryonic window" in adults via a series of skin disruptions, stimulating stem cells causing new hair follicles to grow. We believe that Follica's technology is the first observed to create new follicles of hair, followed by the application of specific compounds to enhance the effort.

Program discovery process by the PureTech team

- We were interested in conditions of aging and focused on hair follicles given their importance in regulating human hair and skin rejuvenation across many medical conditions. We engaged leading dermatologists and hair follicle experts and identified and in-licensed intellectual property from George Cotsarelis, M.D., the Chair of the Department of Dermatology at the University of Pennsylvania, on hair follicle neogenesis, or HFN, prior to its publication in the journal *Nature*. We translated the academic work into an in-office procedure after testing a number of modalities for initiating HFN, identified and co-invented intellectual property around modalities and drug compounds to enhance the newly formed hair follicles and helped conduct multiple POC studies to prioritize HFN inducing modalities and prioritize potential drug compounds.
- Follica's core technology and patent suite has been developed in collaboration with leading researchers, building on the work of Dr. Cotsarelis. Follica's other key scientific advisors include Richard Rox Anderson, M.D., Chairman of the Wellman Center for Photomedicine at the Massachusetts General Hospital, Ken Washenik, M.D., Ph.D., Medical Director of Bosley and the Executive Vice President of Scientific and Medical Development of the Aderans Research Institute.

Patient need and market potential

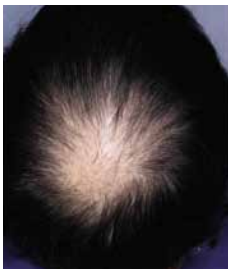
- Androgenetic alopecia represents the most common form of hair loss in men and women, with an estimated 90 million people who are eligible for treatment in the U.S alone. Additionally, the market is estimated to be over $1 billion in the U.S. and $3.5 billion globally. Only two drugs, both of which have demonstrated a 12% increase of non-vellus hair count over baseline for their primary endpoints, are currently approved for the treatment of androgenetic alopecia. The most effective current approach for the treatment of hair loss is hair transplant surgery, comprising a range of invasive, expensive procedures for a subset of patients who have enough donor hair to be eligible. As a result, Follica believes that there is significant unmet need for safe, effective, non-surgical treatments which grow new hair. Follica's regenerative biology platform has potential applications beyond hair growth to other aging-related conditions and wound healing, such as facial skin rejuvenation.

Milestones achieved and development status

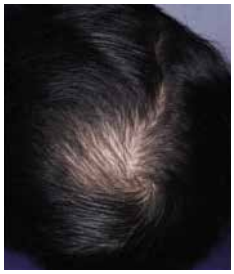
- In January 2021, Follica announced the appointment of two leaders in aesthetic medicine and dermatology to its Board of Directors. Tom Wiggans, former Chief Executive Officer of Dermira, joined as Executive Chairman with over 30 years of experience leading biopharmaceutical companies from the start-up stage to global commercialization, and Michael Davin, former Chief Executive Officer of Cynosure, joined as an Independent Director with over 30 years of experience in the medical device industry.
- In 2021, Follica continued to advance its regenerative biology platform, including preparing for a registration clinical program in male androgenetic alopecia.
- In the three previously conducted clinical studies of patients with androgenetic alopecia, Follica demonstrated hair follicle neogenesis via biopsy following skin disruption and hair growth through target area hair count. One of these studies demonstrated that skin disruption alone generates not only new hair follicles but also terminal (visible, thick) hairs. Follica has been optimizing its device and conducting tests in androgenetic alopecia and other medical indications and is further developing and testing compounds that enhance the newly formed follicles and hairs.
- In December 2019, Follica announced topline results from the safety and efficacy optimization study of its lead candidate to treat hair loss in male androgenetic alopecia. The study was designed to select the optimal treatment regimen using Follica's proprietary device in combination with a topical drug and successfully met its primary endpoint. The selected treatment regimen demonstrated a statistically significant 44% improvement of non-vellus (visible) hair count after three months of treatment compared to baseline ($p < 0.001$, $n = 19$). Across all three treatment arms, the overall improvement of non-vellus hair count after three months of treatment was 29% compared to baseline ($p < 0.001$, $n = 48$), reflecting a clinical benefit across the entire study population and a substantially improved outcome seen with the optimal treatment regimen. Additionally, a prespecified analysis comparing the 44% change in non-vellus hair count to a 12% historical benchmark set by approved pharmaceutical products established statistical significance ($p = 0.005$).

Sample patient outcome from FOL-004 data

Screening



Day 85



Note: Results depicted in the images are above the average demonstrated in the optimization trial.

1 As of December 31, 2021, PureTech's percentage ownership of Follica was approximately 76.0% on an outstanding voting share basis. We have a right to royalty payments as a percentage of net sales from Follica.

2 Therapeutic candidates are investigational and have not been cleared by the FDA for use in the U.S.

3 Follica has an active IND on file with the FDA for FOL-004. Our board designees represent a majority of the members of the board of directors of Follica, but Follica has its own independent management team. In January 2021, Tom Wiggans joined as Executive Chairman and Michael Davin joined as an independent member of the Board of Directors. Mr. Wiggans has over 30 years of experience and most recently co-founded and served as Chairman and Chief Executive Officer of Dermira. Mr. Davin also has over 30 years of experience, including 14 years as Chief Executive Officer at Cynosure. PureTech's role in the development of Follica's therapeutic candidates is through our representation on its board of directors and our role as a majority shareholder. Follica is well-protected with a robust intellectual property portfolio. Follica was incorporated in July 2005.

4 The letters next to the therapeutic candidates denote whether the therapeutic candidate is a pharmaceutical product (P), biologic (B) or device (D).

Milestones achieved and development status (continued)

– The study was an endpoint-blinded, randomized, controlled study designed to establish therapeutic parameters for Follica's proprietary HFN device in combination with a topical on-market drug. The study involved a less than five-minute in-office experimental scalp procedure using the HFN and evaluated the optimal frequency and number of treatments across three arms. The study consisted of 48 men aged 18 to 40 who had moderate grades of androgenetic alopecia as determined by the Hamilton Norwood III-IV scale. The regimen was well tolerated across all treatment arms with no reported SAEs. No AEs were related to device treatment. A single non-severe event (headache) was determined to be related to use of the drug and is in line with minor side effects seen from treatment with the approved drug alone.

Proprietary in-office treatment combines targeted scalp micro-disruption device with a topical on-market drug to create and grow new hairs

- Follica has studied the potential for its proprietary device approach to address other regenerative conditions, including female pattern hair loss and facial skin rejuvenation.

Expected milestones

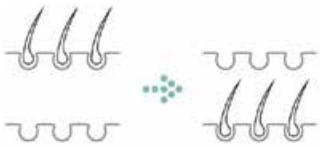
- Follica plans to initiate a registration clinical program in male androgenetic alopecia in 2022.
- Follica also has proprietary amplification compounds in development and ongoing discovery efforts to expand its pipeline.

Follica's approach

Existing drugs

Thicken and maintain remaining hair

Hair transplant



Moves remaining hair

Follica approach (Device plus drug)

Designed to grow new hair and thicken existing hair

Investigational device and new drug. Limited by United States law to investigational use.

Follica's pipeline

Therapeutic Candidate[3]	Indication	Discovery/Preclinical	Phase 1	Phase 2	Phase 3
FOL-004	Androgenetic alopecia				

Phase in progress Phase completed

SONDE

Founded Entity	PureTech Ownership[1]	Therapeutic Candidate[2,3]		Indication	Stage of Development
Sonde[4]	44.6%	Sonde One for Respiratory	D	Respiratory risk detection and monitoring app	Commercial Release
		Sonde Mental Fitness	D	Monitoring vocal features linked to depression, anxiety, and cognition	Commercial Release

- Sonde is developing a voice-based technology platform that detects voice changes linked to health conditions – like depression and respiratory disease – from changes in voice. Using advanced audio signal processing and machine learning, Sonde senses and analyzes subtle vocal changes due to changes in a person's physiology to provide early health detection and monitoring for depression and respiratory conditions. We believe Sonde's Vocal Biomarker program has demonstrated the potential to screen and monitor for disease using information obtained from an individual's voice on commonly owned devices, such as smartphones and smart speakers, and it has the potential to fundamentally change the way mental and physical health is screened and monitored.

Program discovery process by the PureTech team

- We were interested in new ways to detect and quantify disease in a low- to no-burden manner that could allow for more proactive and potentially effective interventions. We selected vocal features as a leading source of health data for this purpose, particularly given the evolving technology landscape where voice interactions with devices are rapidly increasing and identified and in-licensed proprietary technology from Thomas Quatieri, Ph.D., at MIT's Lincoln Laboratory in May 2016. Pursuant to an exclusive license agreement with Dr. Quatieri, we paid an upfront fee and are obligated to pay annual license maintenance fees, both of which we deem immaterial. Pursuant to the agreement, we are also obligated to pay MIT a low single-digit running royalty of net sales of any commercialized product covered by the agreement and a mid-double-digit running royalty of net sales of any commercialized product of a party that we sublicense. MIT is also eligible to receive milestone payments upon the achievement of specified development, regulatory and commercial milestones. We developed additional, novel intellectual property around this concept and helped advance the technology from an academic concept to a commercially focused technology. A core PureTech team member who played a critical role in founding Sonde is currently the Chief Operating Officer.

Patient need and market potential

- The lag between onset of disease and accurate diagnosis and beginning of treatment can be measured in years for many high-burden health conditions, including depression, multiple sclerosis, Parkinson's disease and respiratory diseases, to name just a few. In the U.S., 42% of adults report experiencing symptoms of anxiety or depression, which represents a four-fold increase from 2019, yet less than 10% of people with a mental health condition receive effective treatment. Studies have shown that health conditions including depression, stress, anxiety, sleepiness/fatigue and certain respiratory conditions can impact vocal features such as smoothness, control, liveliness, energy range and clarity. Near-continuous health information, powered by Sonde's technology, has the potential to improve screening, monitoring and timeliness of treatment of high-cost conditions, broadly improving outcomes and care efficiency.
- Development of effective therapies for central nervous system diseases and disorders is hampered by the high cost and inherent variability of these diseases and the reference diagnostic measures used to characterize them. Objective digital tools that can augment, and perhaps one day replace, the current clinical endpoints with novel measures that can be quantified with more meaningful accuracy and less burden can improve patient enrollment and drug development for a range of important conditions.

Milestones achieved and development status

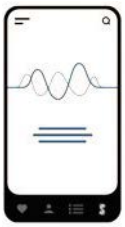
- In October 2021, Sonde announced the launch of Sonde Mental Fitness, a voice-enabled mental health detection and monitoring technology that uses a brief voice sample to evaluate mental well-being. Sonde Mental Fitness is currently available through its API platform for integration into third-party apps. It's also available as a standalone app for iOS and Android, mobile devices to serve as a proof-of-concept for health systems, employers and wellness services interested in testing out the API's capabilities.
- In the January 2022 post-period, Sonde announced the signing of a multi-year strategic partnership with GN Group to research and develop commercial vocal biomarkers for mild cognitive impairment. The research will serve as the backbone for new voice-based tools to help at-risk individuals gain timely and accurate health insights using GN Group's device technologies and, ultimately, to enable early detection and management of life-threatening diseases for the millions of people living with hearing loss.
- In July 2021, Sonde announced its strategic collaboration with leading chipmaker Qualcomm Technologies, Inc. to embed Sonde's vocal biomarker technology into its flagship and high-tier Qualcomm® Snapdragon™ 888 and 778G 5G Mobile Platforms to help bring native, machine learning-driven vocal biomarker capabilities to mobile devices globally. The optimization has the potential to unlock several native health screening and monitoring applications on up to the hundreds of millions of mobile devices that use these Snapdragon mobile platforms.

- **Mental fitness health checks and tracking from 30 seconds of voice on a smartphone**
- **Mental fitness scores based on vocal smoothness, control, liveliness, energy, clarity and crispness**
- **Voice journaling transcribed into text automatically**
- **Recommended mental health content and tips**

- Sonde has collected over one million voice samples from over 80,000 subjects as a part of the ongoing validation of its platform, and it has also initiated research and development to expand its proprietary technology into mental fitness, respiratory disease, and other health, wellness and safety use cases. Sonde has ongoing collaborative partnerships with leading institutions including Montefiore, UCSD, Brigham and Women's Hospital, Albert Einstein College of Medicine, Yale University, Partners Massachusetts General Hospital and multiple other ex-U.S. hospitals, clinics and academic medicine centers.

1 As of December 31, 2021, PureTech's percentage ownership of Sonde was approximately 44.6% on a diluted basis. This calculation includes outstanding shares, options, and warrants, but excludes unallocated shares authorized to be issued pursuant to equity incentive plans.
2 The letters next to the therapeutic candidates denote whether the therapeutic candidate is a pharmaceutical product (P), biologic (B) or device (D).
3 These therapeutic candidates are regulated as devices and their development has been approximately equated to phases of clinical development. Candidates are investigational and have not been cleared by the FDA for use in the U.S.
4 Sonde has obtained Institutional Review Board (IRB) approval independently or in collaboration with partner institutions that covers all past and ongoing human data collection for research in the U.S. and abroad. We have two board designees on the board of directors of Sonde, but Sonde has its own independent management team. Our role in the development of Sonde's therapeutic candidates is through our representation on its board of directors and our role as a majority shareholder. Sonde is well-protected with a robust intellectual property portfolio. Sonde was incorporated in February 2015.

The vocal biomarker platform for health and wellness, population health, corporate wellness, telehealth and remote monitoring services



1

Capture seconds of speech on your app via Sonde's API

2

Sonde analyzes voice samples and provides score

3

Outline tasks/resources for your users to maintain their health

4

Sonde's health tracker provides trending data

Expected milestones

- Sonde plans to launch key pilot programs in the employer wellness, health system and provider space in 2022.

Sonde's pipeline

Therapeutic Candidate[3]		Health Condition	In Development	Product and Clinical Validation	Commercial Release
Sonde App	Sonde Mental Fitness	Monitoring vocal features linked to depression, anxiety, and cognition			
	Sonde One for Respiratory	Respiratory detection and monitoring app			
Sonde API Platform	Respiratory API	Respiratory detection and monitoring			
	Mental Fitness API	Monitoring vocal features linked to depression, anxiety, and cognition			

Phase in progress Phase completed

entrega

Founded Entity	PureTech Ownership[1]	Description[2]	Stage of Development
Entrega	74.3%	Engineering hydrogels to enable the oral administration of biologics	Preclinical

- Entrega is focused on the oral administration of biologics, vaccines and other drugs that are otherwise not efficiently absorbed when taken orally. The vast majority of biologic drugs, including peptides, proteins and other macromolecules are currently administered by injection, which can present challenges for healthcare administration and compliance with treatment regimes. Entrega believes oral administration thus represents an ideal administration approach for this increasingly large class of therapies reshaping many areas of medicine, including the treatment of diabetes.
- Entrega's technology platform is an innovative approach to oral administration which uses a proprietary, customizable hydrogel dosage form to control local fluid microenvironments in the GI tract in an effort to both enhance absorption and reduce the variability of drug exposure.

Program discovery process by the PureTech team	• We were interested in enabling the oral administration of biologics, which has been a long-standing problem in drug development. We engaged with leading experts in drug administration, including Robert Langer, Sc.D., and screened over 100 technologies and the initial platform was licensed from Samir Mitragotri, Ph.D., when he was Professor of Chemical Engineering at UC Santa Barbara (currently Hiller Professor of Bioengineering and Hansjorg Wyss Professor of Biologically Inspired Engineering at Harvard University). We later enhanced this platform with intellectual property developed by our team. • Other scientific and business advisors include Colin Gardner, Ph.D., former Chief Scientific Officer of Transform Pharmaceuticals, former Senior Vice President of Research and Site Head at Johnson & Johnson and formerly Vice President of Pharmaceutical R&D at Merck & Co., Inc., or Merck, Rodney Pearlman, Ph.D., formerly Chief Executive Officer of Nuon Therapeutics, President and Chief Executive Officer of Saegis Pharmaceuticals and Director of Pharmaceutical R&D at Genentech, Robert Armstrong, Ph.D., Co-Founder and Chief Executive Officer of Boston Pharmaceuticals and Mr. Howie Rosen, former President of ALZA.
Milestones achieved and development status	• Entrega continued to advance its platform for the oral administration of biologics, vaccines and other drugs that are otherwise not efficiently absorbed when taken orally. As part of its collaboration with Eli Lilly, Entrega has continued to investigate the application of its peptide administration technology to certain Eli Lilly therapeutic candidates. The partnership has been extended into 2022. • Entrega has also continued advancement of its ENT-100 platform for the oral administration of biologics, vaccines and other drugs that are otherwise not efficiently absorbed when taken orally.
Expected milestones	• Entrega has ongoing discovery efforts to expand its pipeline.

1 As of December 31, 2021, PureTech's percentage ownership of Entrega was approximately 74.3% on a diluted basis. This calculation includes outstanding shares, options, and warrants, but excludes unallocated shares authorized to be issued pursuant to equity incentive plans.

2 The management team of Entrega consists of PureTech employees, and a majority of the board of directors are PureTech designees. These PureTech employees actively manage the day-to-day business activities of Entrega and together with the board of directors of Entrega, which is controlled by PureTech, direct the strategy and decision making in connection with the clinical and regulatory development of Entrega's therapeutic candidates. As a result, we exert substantial control over the clinical and regulatory development of Entrega's therapeutic candidates. Additionally, Entrega's lab and office space is shared with our lab and office space. Entrega is well-protected with a robust intellectual property portfolio. Entrega was incorporated in December 2010.

ESG Report

For PureTech, Environmental, Social and Governance (ESG) means building and maintaining a sustainable business so that we can deliver on our mission to discover, develop and aim to commercialize new therapies for devasting diseases where limited or no treatment options currently exist for patients. It is the hard work and commitment of our internal and external stakeholders that makes the achievement of our mission possible. PureTech recognizes the importance of good governance in delivering ESG outcomes and, accordingly, chartered our ESG Committee chaired by a non-Executive Director, Kiran Mazumdar-Shaw, in 2020 to guide our approach and serve as an internal champion for key initiatives.

In this second edition of our ESG reporting, we are providing increased disclosure as we build a strong and sustainable organization. To that end, we have undertaken peer benchmarking, analyzed the Sustainability Accounting Standards Board (SASB) standard for the biotech and pharmaceutical sector in light of our own activities, and engaged in extensive stakeholder discussion to review ESG best practices for PureTech. We also aligned with the United Nations Sustainable Development Goals (SDGs) to inform our general sustainability framework. This work has validated our overall approach, including with respect to how we report on ESG externally.

What's New

- We have aligned our 2021 reporting with the SASB standard for the biotech and pharmaceutical sector, focusing our disclosure on those topics that are most material to our business as a clinical-stage biopharmaceutical company. **(See pages 85-87 for SASB Index)**
- We have also increased our level of reporting and transparency as we build a strong and sustainable organization. This includes PureTech's first reporting aligned to the Taskforce on Climate-related Financial Disclosure (TCFD) framework. **(See pages 87-89 for TCFD disclosure)**
- We have aligned our ESG framework with the appropriate UN SDGs. **(See page 74 for SDG alignment)**
- We discuss governance topics related to sustainability in the governance section of this report and cross-reference within this section where relevant. **(See pages 90-146 for Governance section)**

Our Approach

Our ESG framework is built around three focus areas, Patients, People and Planet, to help us deliver on our mission, strategy and purpose to advance innovative and differentiated medicines for patients in need.

Our Process

As we continue to grow our business, it is imperative that our ESG report also reflects that growth and is underpinned by our core values. In order to achieve this, we have established a process to identify and address key environmental, social and governance issues that are important to our stakeholders and are relevant to and have a strategic impact on our business. This process is led by the ESG Committee established in 2020, which plays a crucial role in setting our ESG and sustainability priorities.

Process overview

Step 1	Step 2	Step 3	Step 4	Step 5	Step 6
Engage an external ESG consultant for counsel	Identify relevant and current ESG trend and topics	Evaluate the significance of findings from step 2 to our business operation and strategy	Prioritize issues and assess the reporting framework	Integrate findings in business operation and strategy	Report progress within ESG section of the Annual Report

2021 Highlights

This ESG Report contains disclosure of ESG metrics and activities that are relevant to PureTech's business strategy and were evaluated by PureTech's ESG committee. The information in this section builds off of our inaugural 2020 ESG reporting as we continue to develop appropriate benchmarks for our future targets and strategies that will be used to track PureTech's performance across key areas over time.

This ESG disclosure generally includes data from the PureTech level only; however, in accordance with UK rules contained in the Companies Act covering the reporting of energy and emissions data, PureTech reports emissions data on a consolidated basis for the Group (as defined in Note 1 to the financial statements).

Unless otherwise noted, this submission covers our sustainability and ESG approach for the period January 1, 2021 through December 31, 2021.

Patients

27 therapeutic and therapeutic candidates in development, of which

16 are in clinical stage, and

2 taken from inception to FDA and EU regulatory clearances

People

1 of 10 FTSE 250 companies to have a woman CEO[1]

Ranked top **14th** FTSE 250 company by FTSE Women Leaders Review for surpassing Board and leadership gender balance target[1]

44% gender diversity on the Board level[2]

50% cultural diversity on the Board level[3]

$38K committed to charitable contributions and social causes[4]

Planet

85% less energy consumed at the Boston HQ compared to The 2030 Challenge baseline[5]

84% fewer GHG emissions generated at the Boston HQ compared to The 2030 Challenge baseline

1 Source: FTSE Women Leaders Review, 2021.
2 Board composition at March 24, 2022.
3 Board composition at December 31, 2021.
4 In 2021 and through January 2022 post-period, PureTech made charitable contributions to Life Sciences Cares, The Greater Boston Food Bank (GBFB), Lymphatic Education & Research Network (LE&RN), Langer Prize for Innovation & Entrepreneurial Excellence Fellowship, and Fred Hutchinson Cancer Research Center.
5 The 2030 Challenge is a carbon-neutral target issued by the Architecture 2030 in 2006 recommending all new buildings, developments and major renovations to meet a fossil fuel, GHG-emitting, energy consumption performance standard of 70% below the regional (or country) average/median for any specific building type. Boston HQ building data is assessed as a laboratory type building and the data is generated by AppFolio Property Manager, prepared for Related Beal. The current data available is as of December 31, 2020.

Patients

Our commitment to making the world a better place by creating and advancing innovative new medicines

PureTech is a clinical-stage biotherapeutics company dedicated to discovering, developing and commercializing highly differentiated medicines for devastating diseases where limited or no treatment options currently exist for patients. These include inflammatory, fibrotic and immunological conditions, intractable cancers, lymphatic and gastrointestinal diseases and neurological and neuropsychological disorders, among others. It is our unyielding commitment to this mission that we continue to advance our therapeutic candidates in order to deliver innovative and differentiated medicines for patients in need (see pages 35-56 for our Wholly Owned Program overview).

Our research process begins by identifying new medicines where the underlying mechanism is de-risked by validated biology. We then apply our deep development expertise, proprietary platform technologies, and strategic collaborations to solve key challenges in efforts to unlock the value of each asset. Finally, we advance highly innovative and validated programs that have the potential to change the treatment paradigm for a number of serious diseases into therapeutic candidates.

This product innovation framework has generated 27 therapeutics and therapeutic candidates, of which 16 are clinical stage and 2 have gone from inception at PureTech through successful FDA and EU regulatory clearances for marketing.

Safety of clinical trial participants

The safety of participants who enroll in our clinical trials is an extremely high priority. When sponsoring an IND application, we recognize our responsibility both to clinical trial participants and to regulatory agencies. We have detailed protocols in place including Standard Operating Procedure for Adverse Event Reporting, and our employees who are engaged with clinical trials – either as clinical staff or their designee – are responsible for conducting such trials in compliance with good clinical practice.

PureTech is committed to ensuring that all of its clinical trials follow the standards of the International Conference on Harmonisation (ICH) Good Clinical Practice guidelines and the World Medical Association Declaration of Helsinki on the Ethical Principles for Medical Research Involving Human Subjects. The Company applies these standards to all trials conducted by or on its behalf. So that the trials meet these standards, PureTech seeks approval for clinical trials of investigative medicines from independent ethics committees and local regulatory authorities.

To confirm that a patient is aware of risks involved in a clinical trial, we ensure that every patient has voluntarily committed to the trial and has provided informed consent of their willingness to participate. Informed consent requirements are set out in the PureTech Clinical Research Policy.

PureTech relies on the use of human biological specimens in the development of its innovative therapies, and its Human Biological Specimens Policy specifies that collecting, obtaining, storing and using human biological samples requires informed consent, and that PureTech treat both donors and specimens with respect. PureTech's Chief Medical Officer and Chief Scientific Officer are jointly responsible for ensuring that PureTech follows, 1) applicable bioethical principles, and 2) U.S. and applicable international regulatory requirements and standards. In 2021, there were no FDA sponsored inspections related to clinical trial management and pharmacovigilance that resulted in PureTech receiving Voluntary Action Indicated (VAI) and Official Action Indicated (OAI) from FDA.

Drug safety

None of the therapeutic candidates from within PureTech's Wholly Owned Pipeline are currently on the market. In 2021, PureTech received no FDA warning letters, no products were delayed due to a lack of regulatory approval and no product recalls took place.

Equitable pricing, affordability and access

As we progress the therapeutic candidates from within PureTech's Wholly Owned Pipeline toward the market, we are committed to pursuing equitable pricing, affordability and access when those therapeutic candidates get to market, if we are successful in achieving the regulatory approvals or clearances required to launch them. We will routinely conduct comprehensive market research as we advance our therapeutic candidates. We recognize that equitable access to medicines is key to solving many public health issues and will continue to consider factors around equitable access to medicines as we advance our therapeutic candidates.

Animal testing

Animal research plays an essential and currently irreplaceable role in the advancement of healthcare. PureTech conducts animal testing only when necessary to advance the development of therapeutics and is required by regulatory authorities such as the FDA, before human testing of new medicines can take place. Most of our studies involving animals are conducted at external qualified and certified vendors.

We follow the guidelines set out under the USDA Animal Welfare Act and are committed to the humane and ethical treatment of animals: thoughtful use of animals will minimize the number used while producing quality data and providing the greatest benefit to humans. Before using laboratory animals in research, alternatives must be considered.

We apply the 3 Rs standard:

REPLACE	REDUCE	REFINE
Use alternative methods where this is possible	Use the minimum number of animals	Minimize pain, suffering and distress, and improve the welfare of the animals used

People

Our employees are an indispensable asset in driving our mission forward, to deliver medical innovations to patients and create a long-term value for shareholders. We recognize that employee satisfaction is a pillar to our success and hence we have zero-tolerance for behavior and actions that may disrupt the collaborative culture. We instead aim to foster engaging and respectful community.

PureTech is proud of its record of attracting and retaining high-quality talent. We aim to create a workplace that enables high achieving people to be successful while also fostering a collegiate atmosphere. Our employees are predominately located near our headquarters in Boston, MA with three individuals based in London.

As of December 31, 2021, we have total of 95 employees of which 54 employees work in R&D roles while 41 are engaged in general and administrative functions. None of our employees are subject to a collective bargaining agreement or represented by a trade or labor union. We consider our relationship with our employees to be excellent.

In 2021, PureTech conducted its first employee engagement survey to assess current levels of satisfaction and identify how the company can better support employees going forward. The results of the employee survey showed that PureTech performs highly when it comes to encouraging teamwork. The company culture builds agile teams that collaborate cross functionally and remain resilient and committed to the company vision. A high level of trust in management was reported, and PureTech's employees see themselves as purposeful, goal driven and passionate about working to contribute to the company's success.

Employee survey yielded high participation and high satisfaction rates[6]:

- 3.9 — My manager and I have a trusting and respectful relationship
- 3.8 — I work hard with dedication and tenacity and do whatever it takes to overcome obstacles
- 3.5 — I work in an environment where my mistakes are considered an opportunity for me to learn
- 3.9 — Teamwork is encouraged on my team

As a response to findings that indicated employees would appreciate higher levels of information sharing internally, we implemented increased communication from senior leadership, utilizing a range of internal communications approaches. These include:

- Lunch and learn initiatives
- Regular town halls lead by the CEO with open Q&A session
- Email updates
- Intranet updates
- Group conference calls

Employee recruitment

Our Wholly Owned Programs are advancing quickly and the PureTech team is growing rapidly to deliver on our mission to discover, develop and aim to commercialize new therapies for devastating disease where limited or no treatment options currently exist for patients. Our Wholly Owned Programs have enabled us to create new positions and attract new talent, as is evident from the new hires in 2021. Aligned with this, we have also moved away from positions that have historically supported the creation of new Founded Entities.

PureTech employees as at December 31, 2021

Total number of employees	**95**
Employee growth	48%
Employee turnover[7]	25%
Internal promotions	17%

Partnerships and sustainable recruiting

As part of our development of a sustainable and diverse talent pipeline, we source our talent through our outstanding network of world leading scientists and local top tier universities at the heart of the world's biotech hub in Boston, as well as through partnerships with local university cooperative education programs. Co-op programs provide students with opportunities to alternate periods of academic study with several months of full-time employment related to their academic majors and interests. Undergraduate co-op students can join PureTech for six month paid internships in our Research department, adding to our talent acquisition pipeline.

6 Based on 1-5 rating scale
7 As compared to ~45% in the healthcare industry at large, with PureTech's turnover rate further impacted by the continuing shift of business focus to our Wholly Owned Programs

We also seek to attract new talent through participating in annual life science career fairs targeted at graduate MS/PhD students and is committed to developing the next generation of life science professionals that will carry on our mission.

Additionally, we partner with Project Onramp, which facilitates internships for Massachusetts undergraduate students from under-resourced, under-represented group and/or who are first-generation college students, by bringing on paid summer interns in business operations.

PROJECT ONRAMP

Diversity and inclusion

We are committed to a policy of non-discrimination and equal opportunity for all employees and qualified applicants without regard to race, color, religion, gender and gender identity, pregnancy, sexual orientation, national origin, ancestry, age, physical or mental disability, genetic information, veteran status, military service, application for military service or any other status protected by law.

Women employees and women managers as at December 31, 2021

Women employees	45%
Women managers	33%

We strongly believe that diverse board and senior management team generates better performance, retains exceptional talent, and enhances shareholder value. This unwavering commitment has resulted in a top-down approach to secure diversity and inclusion at PureTech (as seen on page 74).

MassBio

In 2021, PureTech became a Mass Bio Open Letter 2.0 signatory, advocating for equity and inclusivity in the healthcare industry. This aims to increase representation of Black, Brown, and Indigenous People of Color (BIPOC) within Massachusetts' life sciences sector.

Pay equity

We are committed to equitable pay. While we do not currently report on the gender pay gap as we are out of scope of the UK's Equality and Human Rights Commission regulation due to the size of our company, we are committed to workplace transparency and equality as seen in our various human capital programs supporting career development, workplace equity, and diversity and inclusion. This mission is reflected strongly on our board and at management level as seen on page 74.

Employee development and retention

We uphold the value of human capital development at PureTech, encouraging managers and employees to discuss job performance and goals on an informal, day-to-day basis alongside formal performance evaluations conducted annually. Regular one-on-ones between employees and supervisors are highly encouraged and facilitate alignment between management and employee expectations and goals.

Employees are able to enter and track their personal development goals on an online portal, which gives visibility to managers to see their team's efforts and progress. This portal is utilized across all departments and is part of PureTech's commitment to supporting employees in their growth and development.

We support the continued development of our employees by providing funding for in person and online programs on a case-by-case basis in areas relevant to their work. Some of the other development trainings include:

HR training

- A mandatory training at onboarding to understand PureTech practices and policies
- Special training based on job function; e.g. employees who perform GxP work are assigned matrices by the Quality Assurance department
- Employee bias training to understand bias at workplace provided by Yamartino Group
- A mandatory annual anti-harassment training provided to all employees by an outside law firm

Health and safety and first aid training

- A mandatory annual safety training provided to all employees in accordance with the Occupational Safety and Health Administration (OSHA)
- An optional first aid training, provided to all employees by Safety Trainers

IT training

- A mandatory annual training, provided to all employees by Risk Management Solutions (RMS)
- A mandatory cybersecurity training provided to all employees, followed by assigned training

PureTech supports the continued development of our employees by providing in person and online trainings in areas relevant to their work. Support for educational programs is available to all employees and considered on a case-by-case basis.

8 Board composition at March 24, 2022.
9 Board composition at December 31, 2021.

Employee benefits

The physical, financial, social and emotional health of our employees is a priority at PureTech. As a result, we provide a range of benefits for employees. Following a US model since this is where the majority of our employees are based, we offer the following perks and benefits:

- Premium health plan with an option to choose from PPO or HMO plan
- Dental plan
- Vision plan
- Short-term disability plan
- Long-term disability plan
- Life insurance
- Medical FSA
- Dependent Care FSA
- Health Reimbursement Account (HRA)
- Benefits continuation (COBRA)
- Paid parental leave (Up to 12 weeks)
- Nursing room
- 401(k) retirement plan with 3% non-elective contribution by the company
- Performance share plan
- 1-on-1 financial coaching
- Technology reimbursement program
- Pre-tax parking and transit benefits
- Gym membership in addition to an onsite gym facility
- Entertainment discounts
- Employee led Social Committee
- Employee led Cultural Committee
- Onsite free snacks & drinks
- Flexibility to work from home

In 2021, some benefits were adjusted in response to the changing nature of work due to COVID-19, for example, gym membership reimbursement eligibility was extended to virtual fitness programs.

PureTech has a performance share plan in place under which the majority of employees are granted stock options upon joining the organization and periodically, to ensure appropriate market-based compensation and incentive alignment with the goals of the organization and its shareholders.

Employee health and safety

The COVID-19 global pandemic that changed the world in 2020 has shifted the way we operate. It is our unyielding commitment to keeping each other and the community safe that has allowed us to implement a COVID-19 action plan and policy. The COVID-19 policy was swiftly drafted and implemented in response to the pandemic, outlining general and special safety procedures based on employee roles, compliance requirements, travel restrictions, exposure responses, and other operational protocols. Additionally, onsite COVID-19 testing requirements were implemented to keep employees, their families, and our community safe.

During 2021, PureTech took steps to evolve its hybrid working model in response to the COVID-19 pandemic, to allow scientists to work onsite safely with minimized risk. To ease the transition to a hybrid model, an online desk booking system was introduced, enabling employees to plan their return to the office flexibly. Other remote operation initiatives included continued utilization of SaaS products to enable employee collaboration, communications and workflow management with minimum disruption.

Employee engagement

We are committed to maintaining and expanding a positive and interconnected company culture. To foster employee engagement and collaboration, the following initiatives were launched in 2021:

Employee intranet

- To provide access to internal and external resources
- To provide online staff directory, spotlighting employee birthdays and work anniversaries
- To serve as a centralized portal for human resources documents

Formation of employee-led Cultural Committee

- To create programs that celebrate diversity, promote equity, and encourage respect for one another

Formation of employee-led Social Committee

- To organize social events to foster a sense of community amongst one another

Community engagement

As a member of the world's top biotech hub in Boston, we are committed to giving back to our community. In 2021 and in January 2021 post-period, we contributed to the following charitable initiatives:

Life Sciences Cares	Life Science Cares is a non-profit organization with a mission to leverage the intellectual, financial, and human capital of the life sciences industry in efforts to reduce the effects of poverty in Boston, Philadelphia, San Diego and the Bay Area.
The Greater Boston Food Bank (GBFB)	GBFB is the largest hunger-relief organization in New England committed to increasing our food distribution by providing three meals a day to every person in need in Eastern Massachusetts while supporting healthy lives and healthy communities. GBFB is a member of Feeding America, the nation's largest hunger-relief organization.
Lymphatic Education & Research Network (LE&RN)	LE&RN is committed to educating the public about lymphatic disease and the need for treatment and research. LE&RN hosts symposiums several times a year in which patients, family members, and the medical community are provided with the opportunity to hear from experts in the field.
Langer Prize for Innovation & Entrepreneurial Excellence Fellowship	Sponsored by the Langer Prize Endowment, the fellowship will award unrestricted grants of up to $100,000 to assist researchers particularly those working in chemical and biological engineering in pursuing "blue-sky" ideas that may lead to important technical and commercial innovations.
Fred Hutchinson Cancer Research Center	Fred Hutchinson Cancer Research Center is dedicated to the elimination of cancer and related diseases as causes of human suffering and death.

Planet

PureTech is committed to managing the environmental impact of its operations, the majority of which relate to business functions at our various locations, business travel and employee commuting.

Streamlined Energy & Carbon Reporting

The section below includes our second year of reporting under the Streamlined Energy & Carbon Reporting requirements. The reporting period is the same as the Group's financial year, January 1, 2021 to December 31, 2021. We observed a slight increase in energy and emissions in 2021 as a result of easing COVID-19 related operation restrictions compared to 2020.

Organization Boundary and Scope of Emissions

We have reported on all the emission sources required under the Companies Act 2006 (Strategic Report and Directors' Reports) Regulations 2018. These sources fall within the Group's consolidated financial statement.

An operational control approach has been used in order to define our organizational boundary. This is the basis for determining the Scope 1, 2 and 3 emissions for which the Group is responsible.

The emissions sources that constitute our boundary for the year to 31st December 2021 are:

- **Scope 1:** natural gas combustion within boilers and carbon dioxide used in our laboratories;
- **Scope 2:** purchased electricity for our own use; and
- **Scope 3:** business travel, employee commuting and third-party deliveries.

Methodology

For the Group's reporting, the Group has employed the services of a specialist adviser, Verco, to quantify and verify the Greenhouse Gas (GHG) emissions associated with the Group's operations.

The following methodology was applied by Verco in the preparation and presentation of this data:

- The Greenhouse Gas Protocol published by the World Business Council for Sustainable Development and the World Resources Institute (the "WBCSD/WRI GHG Protocol");
- Application of appropriate emission factors to the Group's activities to calculate GHG emissions;
- Scope 2 reporting methods – application of location-based and market-based emission factors for electricity supplies;
- Inclusion of all the applicable Kyoto gases, expressed in carbon dioxide equivalents, or CO_2e;
- Presentation of gross emissions as the Group does not purchase carbon credits (or equivalents); and
- Some data for third-party deliverables was not in a usable format and has therefore not been included.

Absolute Emissions

The total Scope 1, 2 and 3 GHG emissions from the Group's operations in the year ending December 31, 2021 were:

- 463.8 tonnes of CO_2 equivalent (tCO_2e) using a 'location-based' emission factor methodology for Scope 2 emissions; and
- 464.4 tonnes of CO_2 equivalent (tCO_2e) using a 'market-based' emission factor methodology for Scope 2 emissions.

Total Energy Use

The total energy use for the Group for FY2021 was 679,127 kWh.

	Electricity/fuel		Mileage	
	Electricity (kWh)	Gas(kWh)	Petrol(kWh)	**Total Energy Use (kWh)**
2021	519,694	85,577	73,856	**679,127**
2020	505,075	133,430	513	**639,018**

Intensity Ratio

As well as reporting the absolute emissions, the Group's GHG emissions are reported below on the metrics of tonnes of CO_2 equivalent per employee and tonnes of CO_2 equivalent per m^2 of occupied space. These are the most appropriate metrics given the majority of emissions result from the operation of the Group's offices and the day-to-day activities of the employees. All of the intensity ratios have been calculated using Scope 1 and Scope 2 emissions only.

The intensity based on floor area is 0.02 tCO_2e per m^2 for both the location-based method and the market-based method. The employee number metric is 0.64 tCO_2e per FTE using the location-based method and the market-based method.

Target and Baselines

Given the comparatively low GHG impact of the Group's operations, the Group's objective is to maintain or reduce its GHG emissions per employee and per square metre of occupied space each year and will report each year whether it has been successful in this regard.

There was an increase in total emissions from the previous year due to an increase in Scope 3 emissions. Scope 1 & Scope 2 emissions did reduce in FY2021. This was due to the lower emissions factors used to calculate the electricity and gas emissions, despite the reduction in use of both.

The employee intensity ratio decreased from 1.05 tCO_2e/employee to 0.64 tCO_2e/employee for both location-based and market-based methods. This was due to an increase in emissions and an increase in the number of employees.

There was no change to the floor area intensity ratio.

Key figures

	2021			2020		
GHG emissions	**Tonnes CO_2e**	**tCO_2e/FTE employee**	**tCO_2e/sq. metre**	**Tonnes CO_2e**	**tCO_2e/FTE employee**	**tCO_2e/sq. metre**
Scope 1[10]	17.7	0.08	0.002	25.9	0.18	0.004
Scope 2[11]	116.4	0.56	0.02	120.9	0.86	0.02
Scope 2[12]	116.9	0.56	0.02	120.9	0.86	0.02
Subtotal (location-based)	134.1	0.64	0.02	146.7	1.05	0.02
Subtotal (market-based)	134.6	0.64	0.02	146.8	1.05	0.02
Scope 3[13]	329.6	–	–	232.7	–	–
Total GHG emissions (Location-based)	463.8	–	–	379.4	–	–
Total GHG emissions (Market-based)	464.3	–	–	379.5	–	–

Efficiency actions undertaken

The Group did not undertake any energy efficiency actions during this financial year.

Understanding the Indirect Environmental Impacts of our Business Activities

The Group's day-to-day operational activities have a limited impact on the environment. We do, however, recognize that the more significant impact occurs indirectly, through the investment decisions we make and the operation of the companies we choose to invest in. The Group therefore considers it important to establish and invest in businesses that comply with existing applicable environmental, ethical and social legislation. It is also important that these businesses can demonstrate that an appropriate strategy is in place to meet future applicable legislative and regulatory requirements and that these businesses can operate to specific industry standards, striving for best practice.

Resource management

In 2021, PureTech engaged Veolia Environment for its hazardous medical waste management. Veolia designs and provides game-changing solutions that are both useful and practical for water, waste and energy management, its Voluntary Protection Programs ('VPP') are rated by OSHA and all staff are HAZWOPER certified. In addition to providing waste management service, Veolia provides PureTech's annual waste data. Data from Veolia shows that PureTech produced 8,371lbs (3,797kg) of biologically and chemically hazardous waste in the course of its research in 2021. The majority of this waste is disposed of through conversion to energy or for fuels blending. Only around 309lbs (140kg) of all waste is sent to landfill or incinerated. Full details of waste generated and treatment methods are shown in the tables below.

PureTech hazardous waste emissions 2021 and 2020 (weight in lbs)

	Hazardous	Non-Hazardous	Regulated Medical Waste	Total
2021	1,061.0	649.0	6,661.0	**8,371.0**
2020	834.0	115.0	5,966.0	**6,915.0**

10 Scope 1 being emissions from the Group's combustion of fuel and operation of facilities.
11 Scope 2 being emissions from electricity (from location-based calculations), heat, steam and cooling purchased for the Group's own use.
12 Scope 2 being emissions from electricity (from market-based calculations), heat, steam and cooling purchased for the Group's own use.
13 Scope 3 being all indirect emissions (not in scope 2) that occur in the value chain of the reporting company, including both upstream and downstream emissions.

PureTech hazardous waste treatment methods 2021 and 2020 (weight in lbs)

	Fuel Blending	Incineration	Treatment/ Stabilization	Waste to energy	Landfill	Recycle	Total
2021	858.0	78.0	133.0	5,775.0	231.0	1,296.0	**8,371.0**
2020	666.0	48.0	160.0	5,567.0	75.0	400.0	**6,915.0**

The increase in waste volume was driven by two major reasons – 1) lab operations were significantly limited in 2020 due to the onset of the global pandemic, and 2) our clinical trial activities increased significantly in 2021 due to the advancing pipeline, with nine ongoing clinical studies within the PureTech's Wholly Owned Pipeline at December 31, 2021, compared to the four clinical studies ongoing as at December 31, 2020.

PureTech will continue to monitor these output levels as part of a commitment to keep hazardous waste to a minimum.

PureTech's energy-efficient headquarters

PureTech's headquarters at Innovation Square, 6 Tide Street in Boston, is a brownfield redevelopment offering many environmental benefits.

Innovation Square consolidates PureTech's laboratory and administrative functions in one building, reducing the need for employees to drive between multiple locations.

The building includes features to further reduce use of motor vehicles, including top-rated (6 out of 6) access to public transport, and storage facilities for 22 bicycles (twice the amount required by LEED for the building's size) with shower and changing facilities.

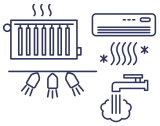
Drivers of electric vehicles (EVs) have access to four charging points in the on-site parking area. Employees are also encouraged to take public transportation to work through a travel subsidy, while an office shuttle bus runs to and from the major Boston train stations.

The building[14] is certified LEED Silver. The fit-out incorporates a range of elements to encourage efficient resource use including:

A roof featuring reflective materials to reduce the building's heat island effect.

Water use reduction of up to 39% through features such as low-flow toilets.

Water-efficient landscaping using hardy and drought tolerant plants to reduce irrigation by 50% over a midsummer baseline case.



Design and model expected to use 35% less energy than the LEED baseline across heating, cooling, lighting, hot water production and other operational functions.

Designed to generate 47% fewer greenhouse gas (GHG) emissions than the AIA 2030 Challenge baseline, equivalent to an annual reduction of 2,500 metric tonnes of CO_2e.

Use of low-emitting flooring, paints and sealants in the construction in compliance with the US SCAQMD Rule #1168 to reduce VOC emissions.

No chlorofluoro-carbon-based refrigerants (CFCs) were used in building heating, ventilation, air conditioning and refrigeration systems.

PureTech's kitchen area is stocked with reusable utensils, plates, cups and glasses to minimize the use of disposable items. Every conference room has recycling bins for paper and other waste, as do all kitchens.

14 All data in this paragraph is taken from the Article 37 Green Building Report and LEED checklist developed by WSP for the building's landlords, Related Beal.

Governance

PureTech's overall governance framework is described in detail in pages 90-146 of this report in compliance with the UK Corporate Governance Code. Additional information relevant to our consideration of ESG matters is provided here.

Governance of ESG

PureTech's ESG committee, chaired by non-executive director Kiran Mazumdar-Shaw, is charged to manage, review and advance ESG issues within the business and drive enhanced reporting through the ESG report each year. The Board, through the ESG committee as led by the committee's Chair and another member of our Board, welcomes active engagement with, and will continue to solicit feedback from, shareholders – and other stakeholders – on matters relating to ESG and corporate stewardship. The ESG committee is supported by at least one management member and a dedicated internal working group.

Business ethics

PureTech strives to maintain the highest level of general business ethics, and to uphold its reputation for integrity and excellence, and maintain the trust of the public and its shareholders, which requires careful observance of the spirit, letter and intent of all applicable laws and regulations, as well as a scrupulous regard for the highest standards of conduct and personal integrity. Therefore, it is important that everyone who works at or for PureTech understands and abides by PureTech's Code of Business Conduct and Ethics (the "Code") which is set out for all staff in the employee handbook.

Board diversity

2021 PureTech Board and Executive Committee composition

44% gender diversity on the Board level[15]

50% cultural diversity on the Board level[16]

The 2021 FTSE Women Leaders Review reported that only 10 companies within the FTSE 250 had women CEOs. PureTech's Founder and CEO, Daphne Zohar, is a successful entrepreneur who assembled a leading team to implement her vision for the Company. Ms. Zohar has been a key participant in fundraising, business development and establishing the underlying programs and platforms that has resulted in PureTech's Wholly Owned Programs and pipelines of PureTech's Founded Entities.

In 2019, we had already achieved the Parker Review's "One by 2021" minimum recommendation that FTSE 350 companies have at least one Board member from an ethnic minority background by 2021.

In 2021, we met FTSE Women Leaders Review's increased gender diversity target recommending FTSE 350 companies to achieve a minimum of 40% women on Boards and in Leadership teams by the end of 2025.

Anti-bribery and corruption

PureTech takes a zero-tolerance approach to bribery and corruption and implements and enforces effective systems to counter bribery. PureTech is bound by the laws of the UK, including the Bribery Act 2010, and has implemented policies and procedures based on such laws. In addition, PureTech has a whistleblowing policy under which staff are encouraged to report to the CEO any alleged wrongdoing, breach of legal obligation or improper conduct by or on the part of the Group or any officers, Directors, employees, consultants or advisors of the Group. PureTech's Audit Committee is satisfied that the policy has been designed to encourage staff to report suspected wrongdoing as soon as possible, to provide staff with guidance on how to raise those concerns and to assure staff that they should be able to raise genuine concerns without fear of reprisals, even if such concern turns out to be mistaken. PureTech has not been involved in any legal proceedings or suffered monetary losses as a result of legal proceedings related to corruption and bribery to date.

Code of ethics governing interactions with health care professionals

PureTech maintains a policy to ensure that interactions and business relationships with health care professionals (HCPs) are conducted in accordance with applicable regulations and ethical standards. This policy provides, among other things, that (a) HCPs will be selected solely on the basis of their qualifications and (b) payments will be made at fair market value taking into account purchasing history or volume or prospective ability to drive sales. The policy provides the roadmap for engagement of HCPs and regulates interactions between PureTech and HCPs.

Grievance reporting and escalation

PureTech's employee handbook clearly states that PureTech prohibits all forms of harassment and offensive conduct, including sexual harassment and any other form of harassment based on protected characteristics, and that we are committed to providing a workplace free of harassment and offensive conduct. The handbook clearly defines and provides examples of the prohibited behavior and strongly encourages employees to report offensive conduct in the workplace to either their supervisor or Human Resources.

All PureTech employees are required to complete a mandatory harassment training with the goal for PureTech to provide an overview of the law and PureTech policies, help employees recognize and stop problem behavior, cultivate a respectful environment where civil conduct is the norm, and enable employees to understand the mechanisms for reporting and responding to inappropriate conduct.

The responsibility to investigate grievances has been assigned to company President, Bharatt Chowrira. Additionally, PureTech provides access to the company's external legal representative and an anonymous helpline to aid the reporting process. There is an opportunity to further develop grievance procedures established in 2021 as we look forward into 2022.

15 Board composition at March 24, 2022.
16 Board composition at December 31, 2021.

Data privacy and security

In circumstances where we are required to collect personal data from patients (or other groups such as employees or customers), PureTech maintains and protects this data by collecting only what is needed and storing it in a way that protects it from intentional or accidental disclosure. We will only make disclosures when we have consent or are required to do so by appropriate legal or regulatory authorities.

Human rights and modern slavery

The Modern Slavery Act 2015 requires organizations conducting business in the UK with worldwide revenues of at least £36 million are required to publish a transparency statement describing the steps they have taken in the last financial year to ensure their business and supply chains are free from modern slavery and human trafficking. PureTech is exempt from this as we do not meet the revenue threshold.

However, we are reviewing, identifying and implementing improvements across our policies as we continue to grow our business. We are strengthening our supplier policies in 2022 with the goal to implement a supplier code of conduct by December 31, 2022.

Supply chain management

PureTech is a clinical stage company and therefore does not have a supply chain at this stage. Amongst the Tier I suppliers who provide materials for our clinical development, 50% participate in Rx-360 International Pharmaceutical Supply Chain Consortium equivalent audit programs. Our Supplier Audit Policy outlines the guidelines on conducting supplier audits to verify a supplier's compliance to regulatory requirements and the supplier's internal documentation, so that the supplied goods and services are produced and provided per PureTech specifications are consistently achieved.

Our Commitment to ESG

PureTech takes pride in its commitment to the community that it consists of (its people), the community it serves (its patients) and the community that it participates within (the world at large). Our team is committed to further our mission of delivering therapeutics where there is unmet need, and we believe this can only be achieved through building a sustainable business.

We believe that the environmental, social and governance initiatives we have undertaken set us on the path towards a brighter future and reporting our ESG metrics helps to orient PureTech along that path.

Appendix

We are aligning our efforts and reporting to recognize the following ESG standards where appropriate:

- The Sustainability Accounting Standards Board (SASB)
- Task Force on Climate-Related Financial Disclosures (TCFD)

SASB Index

The Sustainability Accounting Standards Board (SASB) is an independent, standards-setting US organization that aims to increase consistency in environmental, social and governance (ESG) reporting by sector and has been developed in conjunction with investors. PureTech has chosen to report this first disclosure in 2021 through the lens of the voluntary SASB framework for our industry, biotechnology and pharmaceuticals. We believe that this will provide transparency to investors and other stakeholders. We provide a rationale in instances where SASB recommendations are not applicable to our business model given that stage of the company. We are continually improving our data collection and coordination across our operations in support of our commitment to strengthen our reporting processes and disclosures in the coming years.

Topic	Accounting Metric	Category	Unit of measure	SASB Code	Disclosure Location/ Rationale For Omission
Safety of Clinical Trial Participants	Discussion, by world region, of management process for ensuring quality and patient safety during clinical trials	Discussion and Analysis	–	HC-BP-210a.1	Page 75 – Safety of clinical trial participants
	Number of FDA Sponsor Inspections related to clinical trial management and pharmacovigilance that resulted in: (1) Voluntary Action Indicated (VAI) and (2) Official Action Indicated (OAI)	Quantitative	Number	HC-BP-210a.2	Page 75 – Safety of clinical trial participants
	Total amount of monetary losses as a result of legal proceedings associated with clinical trials in developing countries	Quantitative	Reporting currency	HC-BP-210a.3	N/A There has not been any legal proceedings
Access to Medicines	Description of actions and initiatives to promote access to health care products for priority diseases and in priority countries as defined by the Access to Medicine Index	Discussion and Analysis	n/a	HC-BP-240a.1	N/A PureTech is a clinical stage biopharmaceutical company and has no products on the market from within our Wholly Owned Pipeline
	List of products on the WHO List of Prequalified Medicinal Products as part of its Prequalification of Medicines Program (PQP)	Discussion and Analysis	n/a	HC-BP-240a.2	N/A PureTech is a clinical stage biopharmaceutical company and has no products on the market from within our Wholly Owned Pipeline
Affordability & Pricing	Number of settlements of Abbreviated New Drug Application (ANDA) litigation that involved payments and/or provisions to delay bringing an authorized generic product to market for a defined time period	Quantitative	Number	HC-BP-240b.1	N/A PureTech is a clinical stage biopharmaceutical company and has no products on the market from within our Wholly Owned Pipeline
	Percentage change in: (1) average list price and (2) average net price across U.S. product portfolio compared to previous year	Quantitative	Percentage (%)	HC-BP-240b.2	N/A PureTech is a clinical stage biopharmaceutical company and has no products on the market from within our Wholly Owned Pipeline
	Percentage change in: (1) list price and (2) net price of product with largest increase compared to previous year	Quantitative	Percentage (%)	HC-BP-240b.3	N/A PureTech is a clinical stage biopharmaceutical company and has no products on the market from within our Wholly Owned Pipeline

Topic	Accounting Metric	Category	Unit of measure	SASB Code	Disclosure Location/ Rationale For Omission
Drug Safety	List of products listed in the Food and Drug Administration's (FDA) MedWatch Safety Alerts for Human Medical Products database	Discussion and Analysis	n/a	HC-BP-250a.1	Page 75 – Overview
	Number of fatalities associated with products as reported in the FDA Adverse Event Reporting System	Quantitative	Number	HC-BP-250a.2	N/A PureTech is a clinical stage biopharmaceutical company and has no products on the market from within our Wholly Owned Pipeline
	Number of recalls issued; total units recalled	Quantitative	Number	HC-BP-250a.3	N/A PureTech is a clinical stage biopharmaceutical company and has no products on the market from within our Wholly Owned Pipeline
	Total amount of product accepted for takeback, reuse, or disposal	Quantitative	Metric tons (t)	HC-BP-250a.4	N/A PureTech is a clinical stage biopharmaceutical company and has no products on the market from within our Wholly Owned Pipeline
	Number of FDA enforcement actions taken in response to violations of current Good Manufacturing Practices (CGMP), by type	Quantitative	Number	HC-BP-250a.5	N/A PureTech is a clinical stage biopharmaceutical company and has no products on the market from within our Wholly Owned Pipeline
Counterfeit Drugs	Description of methods and technologies used to maintain traceability of products throughout the supply chain and prevent counterfeiting	Discussion and Analysis	n/a	HC-BP-260a.1	N/A PureTech is a clinical stage biopharmaceutical company and has no products on the market from within our Wholly Owned Pipeline
	Discussion of process for alerting customers and business partners of potential or known risks associated with counterfeit products	Discussion and Analysis	n/a	HC-BP-260a.2	N/A PureTech is a clinical stage biopharmaceutical company and has no products on the market from within our Wholly Owned Pipeline
	Number of actions that led to raids, seizure, arrests, and/or filing of criminal charges related to counterfeit products	Quantitative	Number	HC-BP-260a.3	N/A PureTech is a clinical stage biopharmaceutical company and has no products on the market from within our Wholly Owned Pipeline
Ethical Marketing	Total amount of monetary losses as a result of legal proceedings associated with false marketing claims	Quantitative	Reporting currency	HC-BP-270a.1	N/A PureTech is a clinical stage biopharmaceutical company and has no products on the market from within our Wholly Owned Pipeline
	Description of code of ethics governing promotion of off-label use of products	Discussion and Analysis	n/a	HC-BP-270a.2	N/A PureTech is a clinical stage biopharmaceutical company and has no products on the market from within our Wholly Owned Pipeline
Employee Recruitment, Development & Retention	Discussion of talent recruitment and retention efforts for scientists and research and development personnel	Discussion and Analysis	n/a	HC-BP-330a.1	Pages 76-78 – Employee recruitment
	(1) Voluntary and (2) involuntary turnover rate for: (a) executives/senior managers, (b) midlevel managers, (c) professionals, and (d) all others	Quantitative	Rate	HC-BP-330a.2	Page 76 – Employee recruitment

Topic	Accounting Metric	Category	Unit of measure	SASB Code	Disclosure Location/ Rationale For Omission
Supply Chain Management	Percentage of (1) entity's facilities and (2) Tier I suppliers' facilities participating in the Rx-360 International Pharmaceutical Supply Chain Consortium audit program or equivalent third-party audit programs for integrity of supply chain and ingredients	Quantitative	Rate	HC-BP-430a.1	Page 84 – Supply chain management
Business ethics	Total amount of monetary losses as a result of legal proceedings associated with corruption and bribery	Quantitative	Reporting currency	HC-BP-510a.1	Page 83 – Anti-bribery and corruption; whistleblowing
	Description of code of ethics governing interactions with health care professionals	Discussion and Analysis	n/a	HC-BP-510a.2	Page 83 – Code of ethics governing interactions with health care professionals

TCFD Disclosure

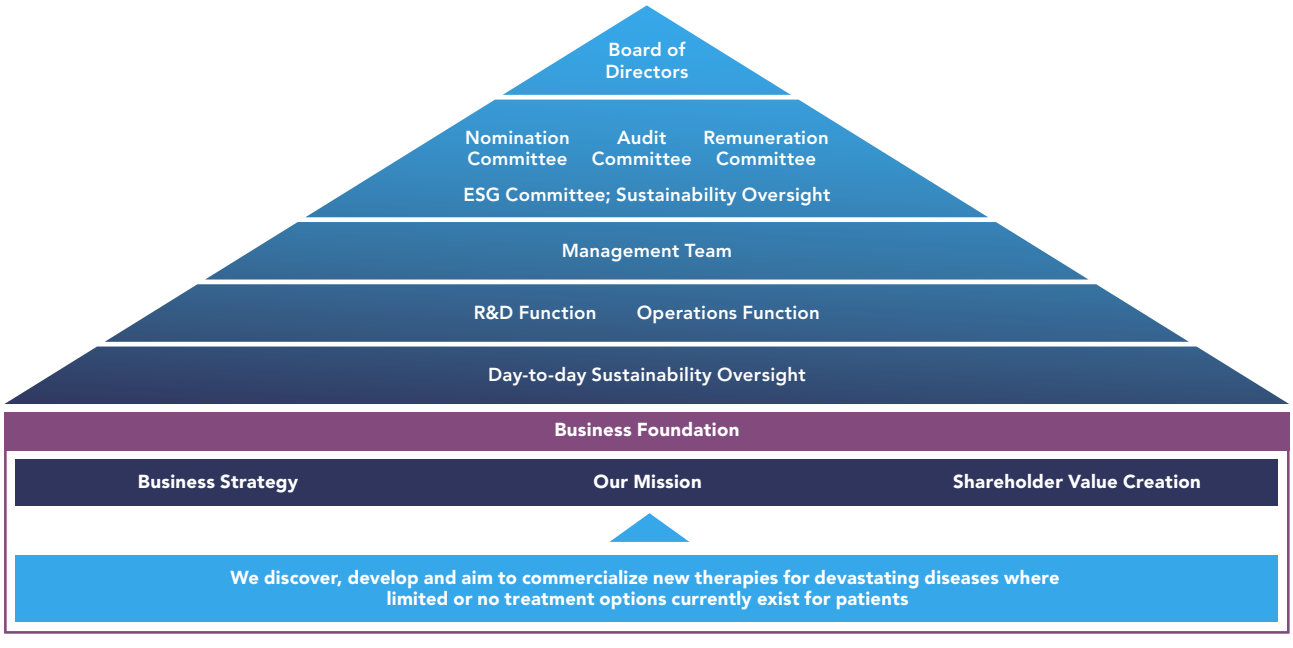
The Task Force on Climate-related Financial Disclosures (TCFD) was created in 2015 by the UK Financial Stability Board (FSB) to develop consistent climate-related financial risk disclosures for use by companies, banks, and investors in providing information to stakeholders. Here we provide our 2021 disclosure in accordance with the TCFD framework.

Overview

PureTech recognizes that the social and environmental sustainability of our operating model and the ability to manage the potential impacts of climate change on our business and strategic plans are among the factors that are integral to the long-term success of our business. This section provides PureTech's first report aligned to the TCFD guidelines, which are based on the recommendations set out by the UK Financial Stability Board to address any potential climate and sustainability related impacts that are identified as relevant to our business through the implementation of forward strategic thinking and action plans. While our day-to-day impact on the environment and the environment's day-to-day impact on us is limited as a result of the current scale of our operations and phase of our business, we recognize the importance of mitigating long-term risks for the benefit of society and our business, especially as our business grows over the coming years. PureTech is committed to managing the climate impact of our operations, the majority of which currently relate to business functions at our various locations, business travel and commuting. Informed by key thought leaders on this emerging reporting requirement, this section describes our process and actions as of December 31, 2021.

Governance

As discussed elsewhere in our Annual Report and Accounts, PureTech's Board of Directors is charged with formal risk identification and with implementing appropriate procedures and strategies for risk mitigation and management, including through quarterly discussions of the key risks facing PureTech. The Board utilizes its risk management framework to help guide PureTech's overall strategy, major plans of action, corporate policies and business plans and objectives, which are then implemented by PureTech's management team with Board oversight and advice. See pages 117-120 in the 2021 Annual Report and Accounts for further details related to the Board roles and responsibilities and pages 90-93 related to the Board's risk management framework and processes.



In 2020, PureTech's Board of Directors formed an ESG Committee, chaired by Non-Executive Director, Kiran Mazumdar-Shaw. Ms. Mazumdar-Shaw has extensive expertise on climate-related risk management as seen from her role as the ESG committee chair at Infosys and Syngene. Additionally, Biocon, which Ms. Mazumdar-Shaw is the founder and Executive Chairperson of has most recently been added to DJSI Emerging Market index for its ESG practices. The role of the ESG committee is to manage, review and advance ESG issues within the business, a role that includes assessing and overseeing climate-related risks and opportunities, as well as considering how such risks and opportunities can inform operational and strategic planning for the organization as applicable. The ESG Committee also includes one member of our executive management team and a dedicated working group of internal cross-functional resources, and it is supported by several third party experts. Through this framework, the ESG Committee formally reports on its activities to the full PureTech Board on a regular basis at scheduled meetings. The progress of the Company's ESG initiatives are reported on an annual basis in the Company's Annual Report and Accounts. See pages 73-84 for the 2021 ESG Report.

Strategy

PureTech has undertaken analyses to identify climate-related risks with the potential to have a strategic impact on our business. PureTech is a clinical stage biopharmaceutical company with currently no drugs on the market. Given the nature of our mission and the scope and scale of our current and near-term future operations, PureTech has determined that we do not face any physical and transition risks in the next 12-24 months. We will continue our broad-based risk assessment and we have identified the following specific climate-related risk areas and potential associated financial impacts that we intend to monitor over time as part of our risk management process (for short, medium and long-term risk):

- Transitional and Market: Increased operating costs due to the introduction of carbon pricing/taxation schemes or other supply-chain cost increases
- Physical and Market: Supply chain or operational disruption or increased operational costs due to increased severity of extreme weather events or long-term changes to weather patterns
- Transitional and Reputational: Potential impacts to reputation if PureTech falls short of stakeholder expectations
- Transitional and Legal and Reputational: Increased costs of compliance with new regulations associated with climate-related reporting obligations

In the short-term, we intend to implement formal business continuity plans in the next 12 months to ensure our physical operations and supply chains are mitigating risks and potential impacts of business interruptions. As we look into the future, we will continue to monitor climate-related risks and opportunities that impacts our operations and will also consider performing scenario analysis to assess transition and physical risk when the state of operations is sufficiently advanced to render such analysis meaningful for ~5 year long-term strategic planning.

Similar to our assessment of risks, we have not identified any specific material opportunities with the potential to impact our business model. However, we will continue our analysis over time, especially in the following areas (for short, medium and long-term opportunities):

- Market: Reducing operating costs through energy-efficient improvements
- Transitional and Reputational: Opportunities with respect to being early-adopter of enhanced disclosure measures or lower-carbon technologies

Risk Management

As previously noted, we discuss our overall risk management processes elsewhere in our ARA (please see the section captioned "Risk Management" on pages 90-93), which processes are inclusive of our assessment of climate-related risks. While climate-related risks have not been identified as a principal risk for PureTech at this time, we intend to continue to monitor PureTech's climate-related risk profile based on changing external and internal circumstances. Risks are formally identified by the Board and appropriate processes are put in place to monitor and mitigate them on an ongoing basis. PureTech is committed to the introduction of climate risk tools and processes to identify and manage climate related risks as well as control those risks by 2025. In addition, our ESG committee, with the assistance of third-party advisors, has specifically considered climate-related risks on at least an annual basis or more often as the need arises. All findings have been reported and will continue to be reported to the Board.

As part of climate-related monitoring, PureTech employs external services to audit and report on climate-related metrics, including the following assessments more fully discussed in our 2021 ESG Report on pages 80-82:

- Streamlined Energy and Carbon Reporting (SECR) prepared by Verco
- Green Building Report and LEED Checklist prepared by WSP in conjunction with the landlord for our headquarters facility, Related Beal
- Hazardous Waste Report prepared by Veolia Environnement S.A.

These findings inform the ESG Committee's climate risk analysis to help identify, and if relevant mitigate, any physical and transition risks considered that may be considered material to the Company. The ESG Committee reports these findings to the Board periodically, and annually at minimum, to enable an understanding of our current situation and to provide data points for the Board to consider as it assesses risks and considers mitigation and/or other strategies. In addition, all employees of PureTech are encouraged to provide suggestions in terms of how to address areas of risk, including climate-related risk, through routine full-company town hall meetings and frequent interactions with leadership in smaller teams.

Metrics and Targets

PureTech employs the services of a specialist adviser, Verco, to quantify and verify the GHG emissions associated with our operations and reports on all of the emission sources required under the Companies Act 2006 (Strategic Report and Directors' Reports) Regulations 2018.

An operational control approach is used in order to define our organizational boundary. This is the basis for determining the Scope 1, 2 and 3 emissions. The emissions sources that constitute our boundary are:

- Scope 1: natural gas combustion within boilers and carbon dioxide used in our laboratories;
- Scope 2: purchased electricity for our own use; and
- Scope 3: business travel, employee commuting and third-party deliveries.

Other environmental-related measures PureTech reports on may be found in our 2021 ESG Report on pages 73-84, which report is not incorporated by reference to this Annual Report. PureTech will consider whether additional metrics may be developed and added over time.

Given (a) the nature of our industry, business operations and therapeutic mission, (b) the fact that PureTech is a clinical stage company with no current supply chain emissions, and (c) that we have not identified any material climate-related risks to our business, PureTech has not set any emissions-related targets, such as a net-zero supply chain, for the Company or incorporated targets into our goals or remuneration policies. We will introduce climate-related targets when the state of operations is sufficiently advanced, such as entering a commercial stage, to render such analysis meaningful.

Next steps

PureTech remains committed to being a good corporate citizen, including managing the impact of our operations with respect to climate as well as environmental matters more generally. As our therapeutic pipeline advances to a commercial stage in the future, we intend to (1) enhance climate-related risks and opportunities management, (2) identify and address areas of improvement year by year, and (3) set greenhouse gas emissions targets and measure performance annually, including as compared to past performance.

Risk management

The execution of the Group's strategy is subject to a number of risks and uncertainties. As a clinical-stage biotherapeutics company, the Group operates in an inherently high-risk environment. The overall aim of the Group's risk management effort is to achieve an effective balancing of risk and reward, although ultimately no strategy can provide an assurance against loss.

Risks are formally identified by the Board and appropriate processes are put in place to monitor and mitigate them on an ongoing basis. If more than one event occurs, it is possible that the overall effect of such events would compound the possible effect on the Group. The principal risks that the Board has identified as the key business risks facing the Group are set out in the table below along with the consequences and mitigation of each risk. These risks are only a high-level summary of the principal risks affecting our business; any number of these or other risks could have a material adverse effect on the Group or its financial condition, development, results of operations, subsidiary companies and/or future prospects. Further information on the risks facing the Group can be found on pages 217 to 251, which also includes a description of circumstances under which principal and other risks and uncertainties might arise in the course of our business and their potential impact.

Risk	Impact*	Management Plans/Actions
1 Risks related to science and technology failure The science and technology being developed or commercialized by some of our businesses may fail and/or our businesses may not be able to develop their intellectual property into commercially viable therapeutics or technologies. There is also a risk that certain of the businesses may fail or not succeed as anticipated, resulting in significant decline of our value.	The failure of any of our businesses could decrease our value. A failure of one of the major businesses could also impact the perception of PureTech as a developer of high value technologies and possibly make additional fundraising at PureTech or any Founded Entity more difficult.	Before making any decision to develop any technology, extensive due diligence is carried out that covers all the major business risks, including technological feasibility, market size, strategy, adoption and intellectual property protection. A capital efficient approach is pursued such that some level of proof of concept has to be achieved before substantial capital is committed and thereafter allocated. Capital deployment is generally tranched so as to fund programs only to their next value milestone. Members of our Board serve on the board of directors of several of the businesses so as to continue to guide each business's strategy and to oversee proper execution thereof. We use our extensive network of advisors to ensure that each business has appropriate domain expertise as it develops and executes on its strategy and the R&D Committee of our Board reviews each program at each stage of development and advises our Board on further actions. Additionally, we have a diversified model with numerous assets such that the failure of any one of our businesses would not result in a failure of all of our businesses.
2 Risks related to clinical trial failure Clinical trials and other tests to assess the commercial viability of a therapeutic candidate are typically expensive, complex and time-consuming, and have uncertain outcomes. Conditions in which clinical trials are conducted differ, and results achieved in one set of conditions could be different from the results achieved in different conditions or with different subject populations. If our therapeutic candidates fail to achieve successful outcomes in their respective clinical trials, the therapeutics will not receive regulatory approval and in such event cannot be commercialized. In addition, if we fail to complete or experience delays in completing clinical tests for any of our therapeutic candidates, we may not be able to obtain regulatory approval or commercialize our therapeutic candidates on a timely basis, or at all.	A critical failure of a clinical trial may result in termination of the program and a significant decrease in our value. Significant delays in a clinical trial to support the appropriate regulatory approvals could impact the amount of capital required for the business to become fully sustainable on a cash flow basis.	We have a diversified model such that any one clinical trial outcome would not significantly impact our ability to operate as a going concern. We have dedicated internal resources to establish and monitor each of the clinical programs in order to try to maximise successful outcomes. We also engage outside experts to help design clinical programs to help provide valuable information and mitigate the risk of failure. Significant scientific due diligence and preclinical experiments are done prior to a clinical trial to attempt to assess the odds of the success of the trial. In the event of the outsourcing of these trials, care and attention are given to assure the quality of the vendors used to perform the work.

* When assessing potential impact of a given risk, we looked at the potential effects on our research and development activities, financial health and overall business operations.

Risk	Impact*	Management Plans/Actions
3 Risks related to regulatory approval The pharmaceutical industry is highly regulated. Regulatory authorities across the world enforce a range of laws and regulations which govern the testing, approval, manufacturing, labelling and marketing of pharmaceutical therapeutics. Stringent standards are imposed which relate to the quality, safety and efficacy of these therapeutics. These requirements are a major determinant of whether it is commercially feasible to develop a drug substance or medical device given the time, expertise, and expense which must be invested. We may not obtain regulatory approval for our therapeutics. Moreover, approval in one territory offers no guarantee that regulatory approval will be obtained in any other territory. Even if therapeutics are approved, subsequent regulatory difficulties may arise, or the conditions relating to the approval may be more onerous or restrictive than we expect.	The failure of one of our therapeutics to obtain any required regulatory approval, or conditions imposed in connection with any such approval, may result in a significant decrease in our value.	We manage our regulatory risk by employing highly experienced clinical managers and regulatory affairs professionals who, where appropriate, will commission advice from external advisors and consult with the regulatory authorities on the design of our preclinical and clinical programs. These experts ensure that high-quality protocols and other documentation are submitted during the regulatory process, and that well-reputed contract research organizations with global capabilities are retained to manage the trials. We also engage with experts, including on our R&D Committee, to help design clinical trials to help provide valuable information and maximize the likelihood of regulatory approval. Additionally, we have a diversified model with numerous assets such that the failure to receive regulatory approval or subsequent regulatory difficulties with respect to any one therapeutic would not adversely impact all of our therapeutics and businesses.
4 Risks related to therapeutic safety There is a risk of adverse reactions with all drugs and medical devices. If any of our therapeutics are found to cause adverse reactions or unacceptable side effects, then therapeutic development may be delayed, additional expenses may be incurred if further studies are required, and, in extreme circumstances, it may prove necessary to suspend or terminate development. This may occur even after regulatory approval has been obtained, in which case additional trials may be required, the approval may be suspended or withdrawn or additional safety warnings may have to be included on the label. Adverse events or unforeseen side effects may also potentially lead to product liability claims being raised against us as the developer of the therapeutics and sponsor of the relevant clinical trials. These risks are also applicable to our Founded Entities and any trials they conduct or therapeutic candidates they develop.	Adverse reactions or unacceptable side effects may result in a smaller market for our therapeutics, or even cause the therapeutics to fail to meet regulatory requirements necessary for sale of the therapeutic. This, as well as any claims for injury or harm resulting from our therapeutics, may result in a significant decrease in our value.	We design our therapeutics with safety as a top priority and conduct extensive preclinical and clinical trials which test for and identify any adverse side effects. Despite these steps and precautions, we cannot fully avoid the possibility of unforeseen side effects. To mitigate the risk further we have insurance in place to cover product liability claims which may arise during the conduct of clinical trials.
5 Risks related to therapeutic profitability We may not be able to sell our therapeutics profitably if reimbursement from third-party payers such as private health insurers and government health authorities is restricted or not available because, for example, it proves difficult to build a sufficiently strong economic case based on the burden of illness and population impact. Third-party payers are increasingly attempting to curtail healthcare costs by challenging the prices that are charged for pharmaceutical therapeutics and denying or limiting coverage and the level of reimbursement. Moreover, even if the therapeutics can be sold profitably, they may not be accepted by patients and the medical community. Alternatively, our competitors – many of whom have considerably greater financial and human resources – may develop safer or more effective therapeutics or be able to compete more effectively in the markets targeted by us. New companies may enter these markets and novel therapeutics and technologies may become available which are more commercially successful than those being developed by us. These risks are also applicable to our Founded Entities and could result in a decrease in their value.	The failure to obtain reimbursement from third party payers, as well as competition from other therapeutics, could significantly decrease the amount of revenue we may receive from therapeutic sales for certain therapeutics. This may result in a significant decrease in our value.	We engage reimbursement experts to conduct pricing and reimbursement studies for our therapeutics to ensure that a viable path to reimbursement, or direct user payment, is available. We also closely monitor the competitive landscape for all of our therapeutics and adapt our business plans accordingly. Not all therapeutics that we are developing will rely on reimbursement. Also, while we cannot control outcomes, we try to design studies to generate data that will help support potential reimbursement.

Risk	Impact*	Management Plans/Actions
6 Risks related to intellectual property protection We may not be able to obtain patent protection for some of our therapeutics or maintain the secrecy of its trade secrets and know-how. If we are unsuccessful in doing so, others may market competitive therapeutics at significantly lower prices. Alternatively, we may be sued for infringement of third-party patent rights. If these actions are successful, then we would have to pay substantial damages and potentially remove our therapeutics from the market. We license certain intellectual property rights from third parties. If we fail to comply with our obligations under these agreements, it may enable the other party to terminate the agreement. This could impair our freedom to operate and potentially lead to third parties preventing us from selling certain of our therapeutics.	The failure to obtain patent protection and maintain the secrecy of key information may significantly decrease the amount of revenue we may receive from therapeutic sales. Any infringement litigation against us may result in the payment of substantial damages by us and result in a significant decrease in our value.	We spend significant resources in the prosecution of our patent applications and maintenance of our patents, and we have an in-house patent counsel and patent group to help with these activities. We also work with experienced external attorneys and law firms to help with the protection, maintenance and enforcement of our patents. Third party patent filings are monitored to ensure the Group continues to have freedom to operate. Confidential information (both our own and information belonging to third parties) is protected through use of confidential disclosure agreements with third parties, and suitable provisions relating to confidentiality and intellectual property exist in our employment and advisory contracts. Licenses are monitored for compliance with their terms.
7 Risks related to enterprise profitability We expect to continue to incur substantial expenditure in further research and development activities. There is no guarantee that we will become operationally profitable, and, even if we do so, we may be unable to sustain operational profitability.	The strategic aim of the business is to generate profits for our shareholders through the commercialization of technologies through therapeutic sales, strategic partnerships and sales of businesses. The timing and size of these potential inflows are uncertain. Should revenues from our activities not be achieved, or in the event that they are achieved but at values significantly less than the amount of capital invested, then it would be difficult to sustain our business.	We retain significant cash in order to support funding of our Founded Entities and our Wholly Owned Pipeline. We have close relationships with a wide group of investors and strategic partners to ensure we can continue to access the capital markets and additional monetization and funding for our businesses. Additionally, our Founded Entities are able to raise money directly from third party investors and strategic partners.
8 Risks related to hiring and retaining qualified employees We operate in complex and specialized business domains and require highly qualified and experienced management to implement our strategy successfully. We and many of our businesses are located in the United States which is a highly competitive employment market. Moreover, the rapid development which is envisaged by us may place unsupportable demands on our current managers and employees, particularly if we cannot attract sufficient new employees. There is also the risk that we may lose key personnel.	The failure to attract highly effective personnel or the loss of key personnel would have an adverse impact on our ability to continue to grow and may negatively affect our competitive advantage.	The Board annually seeks external expertise to assess the competitiveness of the compensation packages of its senior management. Senior management continually monitors and assesses compensation levels to ensure we remain competitive in the employment market. We maintain an extensive recruiting network through our Board members, advisors and scientific community involvement. We also employ an executive as a full-time in-house recruiter. Additionally, we are proactive in our retention efforts and include incentive-based compensation in the form of equity awards and annual bonuses, as well as a competitive benefits package. We have a number of employee engagement efforts to strengthen our PureTech community.

Risk	Impact*	Management Plans/Actions
9 Risks related to business, economic or public health disruptions Business, economic or geopolitical disruptions or global health concerns could seriously harm our development efforts and increase our costs and expenses.	Broad-based business, economic or geopolitical disruptions could adversely affect our ongoing or planned research and development activities. For example, the COVID-19 global pandemic resulted in extended shutdowns of certain businesses around the world. More recently, the Russian invasion of Ukraine has created significant economic disruption as a result of sanctions by the International community and the almost complete shutdown of the Ukrainian economy and business, including healthcare, in Ukraine. Global health concerns, such as COVID-19, or geopolitical events, like the invasion of Ukraine, could also result in social, economic, and labor instability in the countries in which we or the third parties with whom we engage operate. We cannot presently predict the scope and severity of any potential business shutdowns or disruptions, but if we or any of the third parties with whom we engage, including the suppliers, clinical trial sites, regulators and other third parties with whom we conduct business, were to experience shutdowns or other business disruptions, our ability to conduct our business in the manner and on the timelines presently planned could be materially and negatively impacted. It is also possible that global health concerns or geopolitical events such as these one could disproportionately impact the hospitals and clinical sites in which we conduct any of our current and/or future clinical trials, which could have a material adverse effect on our business and our results of operation and financial impact.	To date, we have seen limited impact on our research and development activities and the operation of our company more generally, but we will continuously monitor the COVID-19 pandemic and the invasion of Ukraine and their impact on our business going forward. It is possible that we may see further impact as the situation continues to develop. With respect to the COVID-19 pandemic, we have continued to be proactive in limiting the number of staff on site, requiring that all on-site employees test twice a week and providing personal protective equipment to our staff.

Brexit

The United Kingdom withdrew from the European Union on January 31, 2020 (Brexit) and the transition period for such withdrawal ended on December 31, 2020. Although the Board has considered the potential impact of Brexit as part of its risk management, given that we principally operate in the United States and hold substantially all assets in U.S. dollars, we do not believe there have been or will be any material financial effect on our business, or any significant operational issues which have arisen or could arise, as a result of Brexit.

Viability

PureTech Health plc Viability Statement

In accordance with the UK Corporate Governance Code (Governance Code) published in July 2018, the Directors have assessed the prospects of the Company, and with respect to the December 31, 2021, financial position, we have sufficient available funding to extend operations into the first quarter of 2025. This period is deemed appropriate having assessed the financial health as of December 31, 2021. Further, we expect our Wholly Owned Programs (or "Internal segment") to significantly progress during this period and for key Controlled Founded Entities and Non-Controlled Founded Entities to reach significant development milestones over the period of the assessment.

We anticipate our funding to be used to advance our Wholly Owned Programs, to continue research and development efforts, to discover and progress new therapeutic candidates and to fund the Company's head office costs into the first quarter of 2025. We have also reserved capital to support our Founded Entities, should they require it, to reach significant development milestones over the period of the assessment in conjunction with our external partners. It should be noted that the majority of funding has been allocated to the advancement of the Wholly Owned Programs.

The Directors confirm that they have a reasonable expectation that we will continue to operate and meet our obligations as they fall due over the period of the assessment. In making this statement the Directors carried out a robust assessment of the principal risks, including those that would threaten our business model, future performance, solvency or liquidity.

This assessment was made in consideration of our strong financial position, current strategy and management of principal risks. The following facts support the Directors' view of the viability:

- We have significant influence over the spending and strategic direction of our Wholly Owned Programs and Controlled Founded Entities.
- Our business model is structured so that we are not reliant on the successful outcomes of any one therapeutic or technology within the Wholly Owned Programs, or any Controlled Founded Entity or Non-Controlled Founded Entity.

In addition, the fact that the Wholly Owned Programs, Controlled Founded Entities and Non-Controlled Founded Entities (with the exception of Gelesis and Akili) are currently in the research and development stage means that these therapeutics, technologies and entities are not reliant on cash inflows from product sales or services during the period of this assessment. This also means that we are not highly susceptible to conditions in one or more market sectors in this time frame. Although engaging with collaboration partners is highly valuable from a validation and, in some cases, funding perspective, we are not solely reliant on cash flows from such sources over the period of assessment.

Our consolidated cash and cash equivalents as of December 31, 2021, was $465.7 million. Our PureTech Level cash and cash equivalents as of December 31, 2021, was $418.9 million. Our PureTech Level cash and cash equivalents position is highly liquid and is forecasted to support infrastructure costs, Wholly Owned Program research and development activities and the appropriate funding of key Controlled Founded Entities and Non-Controlled Founded Entities, in order to reach significant developmental milestones over the period of the assessment.

The Board reviews the near-term liquidity and regularly considers funding plans of our Wholly Owned Programs, Controlled Founded Entities and Non-Controlled Founded Entities in our assessment of long-term cash flow projections.

While the review has considered all of the principal risks identified, the Board is focused on the pathway to regulatory approval of each therapeutic candidate being developed within our Wholly Owned Pipeline as well as those of our Founded Entities. Further, the Board has considered milestone and royalty funding based on existing collaboration and partnership arrangements, and the ability of the Wholly Owned Program, and each Controlled Founded Entity and Non-Controlled Founded Entity to enter into new collaboration agreements, all of which could be expected to generate cash in-flows but were not included in the assessment. Additionally, given that spending and investment decisions are largely discretionary, there is management control on reducing discretionary spending if unforeseen liquidity risks arise.

The Directors note that our ownership stakes in the Controlled Founded Entities and Non-Controlled Founded Entities are expected to be illiquid in nature, with the exception of our ownership stakes in Karuna and Vor, which are both publicly traded on Nasdaq as well as Gelesis which recently listed on the New York Stock Exchange on January 14, 2022. See Recent Developments below regarding our Founded Entity Akili potential merger. While we anticipate holding these ownership stakes through the achievement of significant milestones or other events, we will continue to be diligent in exploring monetization opportunities after key value accretion has occurred similar to the execution of the sale of 1,000,000 common shares of Karuna for aggregate proceeds of $118.0 million on February 9, 2021, and the sale of 750,000 common shares of Karuna for an aggregate proceeds of $100.1 million on November 9, 2021. We also expect that certain of these Founded Entities may not be successful and this could result in a loss of the amounts previously invested. However, even in this scenario, our liquidity is expected to remain sufficient to achieve the remaining milestone events and fund infrastructure costs.

The Directors have concluded, based on our strong financial position and readily available cash reserves, that we are highly likely to be able to fund our infrastructure requirements, advance multiple clinical trials within our Wholly Owned Pipeline, including trials in more advanced stages, and contribute the amounts considered necessary for the Controlled Founded Entities and Non-Controlled Founded Entities to reach significant development milestones over the period of the assessment. Therefore, there is a reasonable expectation that we have adequate resources and will continue to operate and meet our obligations over the period of the assessment.

Key Performance Indicators – 2021

The key performance indicators (KPIs) below measure our performance against our strategy. As PureTech's strategy has evolved, new KPIs have replaced older metrics that are no longer representative of our progress.

Amount of funding secured for Founded Entities[1,2]

$731.9m

$709.3m (96.9%) came from third parties

2020: $247.8m
2019: $666.8m
2018: $274.0m
2017: $102.9m

Progress
Karuna, Akili, Gelesis, Vor, Vedanta and Sonde all raised funds in the form of financings and non dilutive grants in 2021, including $709.3 million by third party financial and strategic investors.

Number of programs created for pipeline expansion[2]

2

2020: 3
2019: 1
2018: 1
2017: 1

Progress
In 2021, we expanded our Wholly Owned Pipeline with the acquisition of our Founded Entity, Alivio, and the integration of Alivio's therapeutic candidates, LYT-500 and LYT-503/IMB-150, into the Wholly Owned Pipeline. LYT-503/IMB-150 is being advanced in collaboration with Imbrium Therapeutics, which is responsible for all future development activities and funding for LYT-503/IMB-150.

Proceeds generated from sales of Founded Entity equity[2]

$218.1m

2020: $350.6 million
2019: $9.3 million

Progress
A key component of our strategy is to derive value from the equity growth of our Founded Entities. In 2021, we generated cash proceeds of approximately $218 million from the sales of equity in our Founded Entities, which we intend to use to fund our operations and growth and to further expand and advance our clinical-stage Wholly Owned Pipeline, while still maintaining significant equity ownership.

Number of Wholly Owned Programs advanced through clinical phases[2]

1

2020: 3
2019: 0

Progress
We advanced one of our Wholly Owned Programs, LYT-300, into the clinic in 2021. We initiated a Phase 1 clinical study of LYT-300 in healthy volunteers to evaluate the drug as a potential treatment of neurological and neuropsychological conditions with significant unmet need, such as depression, anxiety, sleep disorders, fragile X tremor-associated syndrome, essential tremor and epileptic disorders, among others.

Number of clinical trial initiations[2]

11

2020: 6
2019: 6

Progress
PureTech initiated five clinical trials, Karuna initiated four clinical trials, Vor initiated one clinical trial and Akili initiated one clinical trial in 2021.

Number of clinical readouts[2]

6

2020: 5
2019: 5

Progress
PureTech (two), Karuna (one), Gelesis (one), and Vedanta (two) reported clinical results from across their pipelines in 2021.

1 Funding figure includes private equity financings, loans and promissory notes, public offerings or grant awards. Funding figure excludes future milestone considerations received in conjunction with partnerships and collaborations. Funding figure does not include Gelesis' gross proceeds of $105.0 million from its January 2022 post-period SPAC merger.
2 Number represents figure for the relevant fiscal year only and is not cumulative.

Financial Review

Reporting Framework

You should read the following discussion and analysis together with our Consolidated Financial Statements, including the notes thereto, set forth elsewhere in this report. Some of the information contained in this discussion and analysis or set forth elsewhere in this report, including information with respect to our plans and strategy for our business and financing our business, includes forward-looking statements that involve risks and uncertainties. As a result of many factors, including the risks set forth on pages 90 to 93 and in the Additional Information section from pages 217 to 251, our actual results could differ materially from the results described in or implied by these forward-looking statements.

Our audited Consolidated Financial Statements as of December 31, 2021 and 2020, and for the years ended December 31, 2021, 2020 and 2019, have been prepared in accordance with UK-adopted International Financial Reporting Standards (IFRS). The Consolidated Financial Statements also comply fully with IFRSs as issued by the International Accounting Standards Board (IASB).

The following discussion contains references to the Consolidated Financial Statements of PureTech Health plc, or the Company, and its consolidated subsidiaries, together the Group. These financial statements consolidate the Company's subsidiaries and include the Company's interest in associates and investments held at fair value. Subsidiaries are those entities over which the Company maintains control. Associates are those entities in which the Company does not have control for financial accounting purposes but maintains significant influence over financial and operating policies. Where the Company has neither control nor significant influence for financial accounting purposes, we recognize our holding in such entity as an investment at fair value. For purposes of our Consolidated Financial Statements, each of our Founded Entities are considered to be either a "subsidiary", an "associate" or an "investment held at fair value" depending on whether PureTech Health plc controls or maintains significant influence over the financial and operating policies of the respective entity at the respective period end date. For additional information regarding the accounting treatment of these entities, see Note 1 to our Consolidated Financial Statements included in this report. For additional information regarding our operating structure, see "—Basis of Presentation and Consolidation" below. Fair value of Investments held at fair value, does not take into consideration contribution from milestones that occurred after December 31, 2021, the value of our interests in our consolidated Founded Entities (Vedanta, Follica, Sonde, and Entrega), our Wholly Owned Programs, or our cash.

Business Background and Results Overview

The business background is discussed from pages 1 to 72, which describe in detail the business development of our Wholly Owned Programs and Founded Entities.

Our ability to generate product revenue sufficient to achieve profitability will depend heavily on the successful development and eventual commercialization of one or more of our wholly-owned or Controlled Founded Entities' therapeutics candidates, which may or may not occur. Our Founded Entities, Gelesis, Inc. ("Gelesis"), and Akili Interactive Labs, Inc. ("Akili"), which we have not controlled since 2019 and 2018, respectively, have products cleared for sale, but our Wholly Owned Programs and our Controlled Founded Entities have not yet generated any meaningful revenue from product sales.

We deconsolidated a number of our Founded Entities, specifically Karuna Therapeutics, Inc. ("Karuna"), Vor Biopharma Inc. ("Vor"), and Gelesis during 2019. We expect this trend to continue into the foreseeable future as our Controlled Founded Entities raise additional funding that reduces our ownership interest. Any deconsolidation affects our financials in the following manner:

- our ownership interest does not provide us with a controlling financial interest;
- we no longer control the Founded Entity's assets and liabilities and as a result we derecognize the assets, liabilities and non-controlling interests related to the Founded Entity from our Consolidated Statements of Financial Position;
- we record our non-controlling financial interest in the Founded Entity at fair value; and
- the resulting amount of any gain or loss is recognized in our Consolidated Statements of Comprehensive Income/(Loss).

We anticipate our expenses to continue to increase proportionally in connection with our ongoing development activities related mostly due to the advancement into late-stage studies of the clinical programs within our Wholly Owned Pipeline and Controlled Founded Entities. In addition, having completed our U.S. listing in November 2020, we have, and will continue, to incur additional costs associated with operating as a public company in the U.S. We also expect that our expenses and capital requirements will increase substantially in the near to mid-term as we:

- continue our research and development efforts;
- seek regulatory approvals for any therapeutic candidates that successfully complete clinical trials;
- add clinical, scientific, operational financial and management information systems and personnel, including personnel to support our therapeutic development and potential future commercialization claims; and
- operate as a U.S. public company.

In addition, our internal research and development spend will increase in the foreseeable future as we may initiate additional clinical studies for LYT-100, LYT-200 and LYT-300, and advance LYT-210, LYT-510 and LYT-500 into the clinic and continue to progress our Glyph™, Orasome™ and Alivio™ technology platforms as well as our meningeal lymphatics research program.

In addition, with respect to our Founded Entities' programs, we anticipate that we will continue to fund a small portion of development costs

by strategically participating in such companies' financings when it is in the best interests of our shareholders. The form of any such participation may include investment in public or private financings, collaboration and partnership arrangements and licensing arrangements, among others. Our management and strategic decision makers consider the future funding needs of our Founded Entities and evaluate the needs and opportunities for returns with respect to each of these Founded Entities routinely and on a case-by-case basis.

As a result, we may need substantial additional funding in the future, following the assessment period described above, to support our continuing operations and pursue our growth strategy until such time as we can generate sufficient revenue from product sales to support our operations, if ever. Until such time we expect to finance our operations through a combination of monetization of our interests in our Founded Entities, collaborations with third parties and also potentially from public or private equity or debt financings or other sources. We may be unable to raise additional funds or enter into such other agreements or arrangements when needed on favorable terms, or at all. If we are unable to raise capital or enter into such agreements as, and when needed, we may have to delay, scale back or discontinue the development and commercialization of one or more of our wholly-owned therapeutic candidates.

Measuring Performance

The Financial Review discusses our operating and financial performance, our cash flows and liquidity as well as our financial position and our resources. The results for each year are compared primarily with the results of the preceding year.

Reported Performance

Reported performance considers all factors that have affected the results of our business, as reflected in our Consolidated Financial Statements.

Core Performance

Core performance measures are alternative performance measures (APM) which are adjusted and non-IFRS measures. These measures cannot be derived directly from our Consolidated Financial Statements. We believe that these non-IFRS performance measures, when provided in combination with reported performance, will provide investors, analysts and other stakeholders with helpful complementary information to better understand our financial performance and our financial position from period to period. The measures are also used by management for planning and reporting purposes. The measures are not substitutable for IFRS results and should not be considered superior to results presented in accordance with IFRS.

Cash flow and liquidity

PureTech Level Cash and Cash Equivalents	**Measure type:** Core performance. **Definition:** Cash and cash equivalents held at PureTech Health plc and only wholly-owned subsidiaries as noted (PureTech LYT, PureTech LYT-100, PureTech Management, Inc., PureTech Health LLC,and other inactive entities in which we have no current operations. During the year ended December 31, 2021, the Company acquired the non controlling interest in Alivio Therapeutics, Inc. and since then Alivio Therapeutics, Inc. is wholly owned by the Company and the related cash and cash equivalents are included in the PureTech Level Cash and Cash Equivalents as of December 31, 2021. The cash and cash equivalents of Alivio Therapeutics, Inc. were not included in the PureTech Level Cash and Cash Equivalents as of December 31, 2020 as during that period, the subsidiary was not wholly owned by the Company. **Why we use it:** PureTech Level Cash and Cash Equivalents is a measure that provides valuable additional information with respect to cash and cash equivalents available to fund the Wholly Owned Programs and make certain investments in Founded Entities.

The Company no longer presents in the reported periods Consolidated Cash Reserves or PureTech Level Cash Reserves as the Company does not have short-term investments in addition to its cash and cash equivalents in all reported periods.

COVID-19

In March 2020, the World Health Organization declared the COVID-19 outbreak a pandemic. The pandemic has since caused widespread and significant disruption to daily life and the global economy as governments have taken actions, including the issuance of stay-at-home orders and social distancing guidelines, and businesses have adjusted their activities. While our business, operations and financial condition and results have not been significantly impacted in 2020 or 2021, as a result of the COVID-19 pandemic, we have taken swift action to ensure the safety of our employees and other stakeholders. We continue to monitor the latest developments regarding the COVID-19 pandemic on our business, operations, and financial condition and results and cannot predict the impact, including as a result of variations of the virus, that the pandemic may have on our business, operations, and financial condition and results.

Recent Developments (subsequent to December 31, 2021)

On January 13, 2022 Gelesis completed its business combination with Capstar Special Purpose Acquisition Corp ("Capstar"). As part of the business combination all shares held in Gelesis, common and preferred, were exchanged for common shares of the merged entity. In addition, PureTech invested $15.0 million in the class A common shares of Capstar as part of the PIPE transaction that took place immediately prior to the closing of the business combination and an additional approximately $5.0 million, as part of the Backstop agreement signed with Capstar on December 30, 2021. Pursuant to the business combination, Gelesis became a wholly-owned subsidiary of Capstar and Capstar changed its name to Gelesis Holdings, Inc., which began trading on the New York Stock Exchange under the ticker symbol "GLS" on January 14, 2022. Following the closing of the business combination, PureTech holds 16,727,582 shares of Gelesis Holdings Inc. common stock, which is equal to approximately 23.2% of Gelesis Holdings Inc's outstanding common shares.

On January 26, 2022 Akili Interactive and Social Capital Suvretta Holdings Corp a special purpose acquisition company announced they had entered into a definitive business combination agreement. Upon completion of the transaction, the combined company's securities are expected to be traded on the Nasdaq Stock Market under the ticker symbol "AKLI". The transaction is expected to close in mid-2022. As part of this transaction the Akili Interactive shares held by the Company will be exchanged for the combined company's securities and the Company's interest in the combined public entity is expected to decrease from its current voting interest in Akili of 26.4%.

Financial Highlights

Following is the reconciliation of the amounts appearing in our Statement of Financial Position to the Alternative Performance Measure described above:

	As of:	
(in thousands)	December 31, 2021	December 31, 2020
Consolidated Cash and cash equivalents	465,708	403,881
Less: Cash and cash equivalents held at non-wholly owned subsidiaries	(46,856)	(54,473)
PureTech Level Cash and Cash Equivalents	$418,851	$349,407

Basis of Presentation and Consolidation

Our Consolidated Financial Information consolidates the financial information of PureTech Health plc, as well as its subsidiaries, and includes our interest in associates and investments held at fair value, and is reported in four operating segments as described below.

Basis for Segmentation

Our Directors are our strategic decision-makers. Our operating segments are based on the financial information provided to our Directors periodically for the purposes of allocating resources and assessing performance. We have determined that each Founded Entity is representative of a single operating segment as our Directors monitor the financial results at this level. When identifying the reportable segments we have determined that it is appropriate to aggregate multiple operating segments into a single reportable segment given the high level of operational and financial similarities across the entities. We have identified multiple reportable segments which are outlined below. Substantially all of our revenue and profit generating activities are generated within the United States and, accordingly, no geographical disclosures are provided.

There was no change to reportable segments in 2021, except the change in the composition of the segments with respect to Alivio, as explained below.

During the year ended December 31, 2021, the Company acquired the non controlling interest in Alivio and since then Alivio is wholly owned by the Company and is managed within the Internal segment. The Company has revised in this report the prior period segment financial information to conform to the presentation as of and for the period ending December 31, 2021. This change in segments reflects how the Company's Board of Directors reviews the Group's results, allocates resources and assesses performance of the Group at this time.

Following is the description of our reportable segments:

Internal

The Internal segment is advancing Wholly Owned Programs, which is focused on immunological, fibrotic and lymphatic system disorders and builds upon validated biologic pathways and proven pharmacology. The Internal segment is comprised of the technologies that are wholly owned and will be advanced through either PureTech Health funding or non-dilutive sources of financing in the near-term. The operational management of the Internal segment is conducted by the PureTech Health team, which is responsible for the strategy, business development, and research and development. As of December 31, 2021, this segment included PureTech LYT, Inc. (formerly Ariya Therapeutics Inc.), PureTech LYT-100, Inc and Alivio Therapeutics, Inc.

Controlled Founded Entities

The Controlled Founded Entities segment is comprised of our subsidiaries that are currently consolidated operational subsidiaries that either have, or have plans to hire, independent management teams and have previously raised, or are currently in the process of raising, third-party dilutive capital. These subsidiaries have active research and development programs and either have entered into or plan to seek a strategic partnership with an equity or debt investment partner, who will provide additional industry knowledge and access to networks, as well as additional funding to continue the pursued growth of the company. As of December 31, 2021, this segment included Entrega, Inc., Follica, Incorporated, Sonde Health, Inc. and Vedanta Biosciences, Inc.

Non-Controlled Founded Entities

The Non-Controlled Founded Entities segment is comprised of the entities in respect of which PureTech Health (i) no longer holds majority voting control as a shareholder and (ii) no longer has the right to elect a majority of the members of the entity's Board of Directors. Upon deconsolidation of an entity the segment disclosure is restated to reflect the change on a retrospective basis, as this constitutes a change in the composition of its reportable segments. The Non-Controlled Founded Entities segment included Akili Interactive Labs, Inc. ("Akili"), Vor Biopharma, Inc. ("Vor"), Karuna Therapeutics, Inc. ("Karuna"), and Gelesis, Inc. ("Gelesis").

The Non-Controlled Founded Entities segment incorporates the operational results of the aforementioned entities to the date of deconsolidation. Following the date of deconsolidation, we account for our investment in each entity at the parent level, and therefore the results associated with investment activity following the date of deconsolidation is included in the Parent Company and Other segment (the "Parent Company and Other segment").

Parent Company and Other

Parent Company and Other includes activities that are not directly attributable to the operating segments, such as the activities of the Parent, corporate support functions and certain research and development support functions that are not directly attributable to a strategic business segment as well as the elimination of intercompany transactions. Parent Company and Other also captures the accounting for our holdings in entities for which control has been lost, which is inclusive of the following items: gain on deconsolidation, gain or loss on investments held at fair value, gain on loss of significant influence, and the share of net loss of associates accounted for using the equity method. As of December 31, 2021, this segment included PureTech Health plc, PureTech Health LLC, PureTech Management, Inc., PureTech Securities Corp., and PureTech Securities II Corp. as well as certain other dormant, inactive and shell entities.

The table below summarizes the entities that comprised each of our segments as of December 31, 2021:

Internal Segment	
PureTech LYT	100.0%
PureTech LYT-100, Inc.	100.0%
Alivio Therapeutics, Inc.	100.0%
Controlled Founded Entities	
Entrega, Inc.	77.3%
Follica, Incorporated	85.4%
Sonde Health, Inc.	51.8%
Vedanta Biosciences, Inc.	48.6%
Non-Controlled Founded Entities	
Akili Interactive Labs, Inc.	26.7%
Gelesis, Inc.	24.5%
Karuna Therapeutics, Inc.	5.6%
Vor Biopharma Inc.	8.6%
Parent Segment[1]	
Puretech Health plc	100.0%
PureTech Health LLC	100.0%
PureTech Securities Corporation	100.0%
PureTech Securities II Corporation	100.0%
PureTech Management, Inc.	100.0%

1 Includes dormant, inactive and shell entities that are not listed here.

Components of Our Results of Operations

Revenue

To date, we have not generated any meaningful revenue from product sales and we do not expect to generate any meaningful revenue from product sales for the near term future. We derive our revenue from the following:

Contract revenue

We generate revenue primarily from licenses, services and collaboration agreements, including amounts that are recognized related to upfront payments, milestone payments, royalties and amounts due to us for research and development services. In the future, revenue may include additional milestone payments and royalties on any net product sales under our collaborations. We expect that any revenue we generate will fluctuate from period to period as a result of the timing and amount of license, research and development services and milestone and other payments.

Grant Revenue

Grant revenue is derived from grant awards we receive from governmental agencies and non-profit organizations for certain qualified research and development expenses. We recognize grants from governmental agencies as grant income in the Consolidated Statement of Comprehensive Income/(Loss), gross of the expenditures that were related to obtaining the grant, when there is reasonable assurance that we will comply with the conditions within the grant agreement and there is reasonable assurance that payments under the grants will be received. We evaluate the conditions of each grant as of each reporting date to ensure that we have reasonable assurance of meeting the conditions of each grant arrangement and it is expected that the grant payment will be received as a result of meeting the necessary conditions.

For proceeds from sale of our investments held at fair value, please see our Consolidated Cash flow Statements, Net cash provided by investing activities.

Operating Expenses

Research and Development Expenses

Research and development expenses consist primarily of costs incurred for our research activities, including our discovery efforts, and the development of our wholly-owned and our Controlled Founded Entities' therapeutic candidates, which include:

- employee-related expenses, including salaries, related benefits and equity-based compensation;
- expenses incurred in connection with the preclinical and clinical development of our wholly-owned and our Founded Entities' therapeutic candidates, including our agreements with contract research organizations, or CROs;
- expenses incurred under agreements with consultants who supplement our internal capabilities;
- the cost of lab supplies and acquiring, developing and manufacturing preclinical study materials and clinical trial materials;
- costs related to compliance with regulatory requirements; and
- facilities, depreciation and other expenses, which include direct and allocated expenses for rent and maintenance of facilities, insurance and other operating costs.

We expense all research costs in the periods in which they are incurred and development costs are capitalized only if certain criteria are met. For the periods presented, we have not capitalized any development costs since we have not met the necessary criteria required for capitalization. Costs for certain development activities are recognized based on an evaluation of the progress to completion of specific tasks using information and data provided to us by our vendors and third-party service providers.

Research and development activities are central to our business model. Therapeutic candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials. We expect that our research and development expenses will continue to increase for the foreseeable future in connection with our planned preclinical and clinical development activities in the near term and in the future. The successful development of our wholly-owned and our Founded Entities' therapeutic candidates is highly uncertain. As such, at this time, we cannot reasonably estimate or know the nature, timing and estimated costs of the efforts that will be necessary to complete the remainder of the development of these therapeutic candidates. We are also unable to predict when, if ever, material net cash inflows will commence from our wholly-owned or our Founded Entities' therapeutic candidates. This is due to the numerous risks and uncertainties associated with developing therapeutics, including the uncertainty of:

- progressing research and development of our Wholly Owned Pipeline, including LYT-100, LYT-200, LYT-210, LYT-300, LYT-510, LYT-500 and continue to progress our Glyph™, Orasome™ and Alivio™ technology platforms as well as our meningeal lymphatics research program and other potential therapeutic candidates based on previous human efficacy and clinically validated biology within our Wholly Owned Programs;
- establishing an appropriate safety profile with investigational new drug application enabling studies to advance our preclinical programs into clinical development;
- the success of our Founded Entities and their need for additional capital;
- identifying new therapeutic candidates to add to our Wholly Owned Pipeline;
- successful enrollment in, and the initiation and completion of, clinical trials;
- the timing, receipt and terms of any marketing approvals from applicable regulatory authorities;
- commercializing our wholly-owned and our Founded Entities' therapeutic candidates, if approved, whether alone or in collaboration with others;
- establishing commercial manufacturing capabilities or making arrangements with third-party manufacturers;
- addressing any competing technological and market developments, as well as any changes in governmental regulations;
- negotiating favorable terms in any collaboration, licensing or other arrangements into which we may enter and performing our obligations under such arrangements;
- maintaining, protecting and expanding our portfolio of intellectual property rights, including patents, trade secrets and know-how, as well as obtaining and maintaining regulatory exclusivity for our wholly-owned and our Founded Entities' therapeutic candidates;
- continued acceptable safety profile of our therapeutics, if any, following approval; and
- attracting, hiring and retaining qualified personnel.

A change in the outcome of any of these variables with respect to the development of a therapeutic candidate

could mean a significant change in the costs and timing associated with the development of that therapeutic candidate. For example, the FDA, the EMA, or another comparable foreign regulatory authority may require us to conduct clinical trials beyond those that we anticipate will be required for the completion of clinical development of a therapeutic candidate, or we may experience significant trial delays due to patient enrollment or other reasons, in which case we would be required to expend significant additional financial resources and time on the completion of clinical development. In addition, we may obtain unexpected results from our clinical trials and we may elect to discontinue, delay or modify clinical trials of some therapeutic candidates or focus on others. Identifying potential therapeutic candidates and conducting preclinical testing and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve product sales. In addition, our wholly-owned and our Founded Entities' therapeutic candidates, if approved, may not achieve commercial success.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries and other related costs, including stock-based compensation, for personnel in our executive, finance, corporate and business development and administrative functions. General and administrative expenses also include professional fees for legal, patent, accounting, auditing, tax and consulting services, travel expenses and facility-related expenses, which include direct depreciation costs and allocated expenses for rent and maintenance of facilities and other operating costs.

We expect that our general and administrative expenses will increase in the future as we increase our general and administrative headcount to support our continued research and development and potential commercialization of our portfolio of therapeutic candidates. We also expect to incur increased expenses associated with being a public company in the United States, including costs of accounting, audit, information systems, legal, regulatory and tax compliance services, director and officer insurance costs and investor and public relations costs.

Total Other Income/(Loss)

Gain on Deconsolidation

Upon losing control of a subsidiary, the assets and liabilities are derecognized along with any related non-controlling interest ("NCI"). Any interest retained in the former subsidiary is measured at fair value when control is lost. Any resulting gain or loss is recognized as profit or loss in the Consolidated Statements of Comprehensive Income/(Loss).

Gain/(Loss) on Investments Held at Fair Value

Investments held at fair value include both unlisted and listed securities held by us, which include investments in Akili, Gelesis, Karuna, Vor and certain insignificant investments. Our ownership in Akili is in preferred shares. Our ownership in Vor was in preferred shares until February 2021 at which time the preferred shares were converted into common shares as part of Vor Initial Public Offering. Preferred shares form part of our ownership in Gelesis and such preferred shares investment is accounted for as Investments Held at Fair value while the investment in common stock is accounted for under the equity method. When the investment in common stock is reduced to zero by equity method losses, subsequent equity method losses are applied to the preferred share investment, which is considered to be a Long-term Interest. Our ownership in Karuna was in preferred shares until its IPO in June 2019 when such shares were converted into common shares. When Karuna's preferred shares converted into common shares, our equity interest in Karuna investment was removed from Investments Held at Fair Value and accounted for under the equity method as we still retained significant influence in Karuna at such time. On December 2, 2019 we lost significant influence in Karuna and, beginning on that date, we accounted for our investment in Karuna in accordance with IFRS 9 as an Investment Held at Fair Value. We account for investments in preferred shares of our associates in accordance with IFRS 9 as Investments Held at Fair Value when the preferred shares do not provide access to returns underlying ownership interests.

Loss Realized on Investments Held at Fair Value

Loss realized on investments held at fair value relates to realized differences in the per share disposal price of a listed security as compared to the per share exchange quoted price at the time of disposal. The difference is attributable to a block sale discount, attributable to a variety of market factors, primarily the number of shares being transacted was significantly larger than the daily trading volume of a given security.

Gain on Loss of Significant Influence

Gain on loss of significant influence relates to the assessment related to the loss of our ability to exert significant influence over an investment in a Non-Controlled Founded Entity that is accounted for under the equity method. For the year ended December 31, 2019, we recognized gain on loss of significant influence in Karuna.

Other Income (Expense)

Other income (expense) consists primarily of gains and losses related to the sale of an asset and certain investments as well as sub-lease income.

Finance Costs/Income

Finance costs consist of loan interest expense and the changes in the fair value of certain liabilities associated with financing transactions, mainly preferred share liabilities in respect of preferred shares issued by our non wholly owned subsidiaries to third parties. Finance income consists of interest income on funds invested in money market funds and U.S. treasuries.

Share of Net Gain (Loss) of Associates Accounted for Using the Equity Method, and Impairment of Investment in Associate

Associates are accounted for using the equity method (equity accounted investees) and are initially recognized at cost, or if recognized upon deconsolidation they are initially recorded at fair value at the date of deconsolidation. The consolidated financial statements include our share of the total comprehensive income and equity movements of equity accounted investees, from the date that significant influence commences until the date that significant influence ceases. When the share of losses exceeds the net investment in the investee, including the investment in preferred shares that are considered Long-term Interests, the carrying amount is reduced to nil and recognition of further losses is discontinued except to the extent that we have incurred legal or constructive obligations or made payments on behalf of an investee.

We compare the recoverable amount of the investment to its carrying amount on a go-forward basis and determine the need for impairment. We recorded an impairment in the common stock investment in Gelesis in the year ended December 31, 2019.

Income Tax

We must make certain estimates and judgments in determining income tax expense for financial statement purposes. The amount of taxes currently payable or refundable is accrued, and deferred tax assets and liabilities are recognized for the estimated future tax consequences attributable to differences between the financial statement carrying amount of existing assets and liabilities and their respective tax bases. Deferred tax assets are also recognized for realizable loss and tax credit carryforwards. Deferred tax assets and liabilities are measured using substantively enacted tax rates in effect for the year in which those temporary differences are expected to be recovered or settled. Net deferred tax assets are not recorded if we do not assess their realization as probable. The effect on deferred tax assets and liabilities of a change in income tax rates is recognized in our financial statements in the period that includes the substantive enactment date.

Results of Operations

The following table, which has been derived from our audited financial statements for the years ended December 31, 2021, 2020 and 2019, included herein, summarizes our results of operations for the periods indicated, together with the changes in those items in dollars:

	Year Ended December 31,				
(in thousands)	**2021**	2020	2019	Change (2020 to 2021)	Change (2019 to 2020)
Contract revenue	**$9,979**	$8,341	$8,688	$1,638	$(347)
Grant revenue	**7,409**	3,427	1,119	3,982	2,308
Total revenue	**17,388**	11,768	9,807	5,621	1,961
Operating expenses:					
General and administrative expenses	**(57,199)**	(49,440)	(59,358)	(7,760)	9,918
Research and development expenses	**(110,471)**	(81,859)	(85,848)	(28,612)	3,988
Operating income/(loss)	**(150,282)**	(119,531)	(135,399)	(30,751)	15,868
Other income/(expense):					
Gain/(loss) on deconsolidation	**—**	—	264,409	—	(264,409)
Gain/(loss) on investments held at fair value	**179,316**	232,674	(37,863)	(53,358)	270,537
Loss realized on sale of investment	**(20,925)**	(54,976)	—	34,051	(54,976)
Gain/(loss) on disposal of assets	**—**	—	—	—	—
Gain on loss of significant influence	**—**	—	445,582	—	(445,582)
Other income/(expenses)	**1,592**	1,035	39	557	996
Other income/(loss)	**159,983**	178,732	672,167	(18,749)	(493,434)
Net finance income/(costs)	**5,050**	(6,115)	(46,147)	11,164	40,032
Share of net gain/(loss) of associates accounted for using the equity method	**(73,703)**	(34,117)	30,791	(39,587)	(64,908)
Impairment of investment in associate	**—**	—	(42,938)	—	42,938
Income/(loss) before income taxes	**(58,953)**	18,969	478,474	(77,922)	(459,504)
Taxation	**(3,756)**	(14,401)	(112,409)	10,645	98,008
Net income/(loss) including non-controlling interest	**(62,709)**	4,568	366,065	(67,277)	(361,497)
Net (loss)/income attributable to the Company	**$(60,558)**	$5,985	$421,144	$(66,543)	$(415,159)

Comparison of the Years Ended December 31, 2021 and 2020

Total Revenue

	Year Ended December 31,		
(in thousands)	**2021**	2020	Change
Contract Revenue:			
Internal Segment	**$8,129**	$5,297	$2,833
Controlled Founded Entities	**1,615**	990	625
Non-Controlled Founded Entities	**—**	—	—
Parent Company and other	**235**	2,054	(1,819)
Total Contract Revenue	**$9,979**	$8,341	$1,638
Grant Revenue:			
Internal Segment	**$1,253**	$1,563	$(310)
Controlled Founded Entities	**6,156**	1,864	4,292
Non-Controlled Founded Entities	**—**	—	—
Parent Company and other	**—**	—	—
Total Grant Revenue	**$7,409**	$3,427	$3,982
Total Revenue	**$17,388**	$11,768	$5,621

Our total revenue was $17.4 million for the year ended December 31, 2021, an increase of $5.6 million, or 47.8 percent compared to the year ended December 31, 2020. The increase was primarily attributable to an increase of $2.8 million in contract revenue in the Internal segment, which was primarily driven by a $6.5 million increase in revenue due to payment

from Imbrium Therapeutics, Inc. following the exercise of the option to acquire an exclusive license for the Initial Product Candidate. The increase was partially offset by a decrease in contract revenue of $3.7 million recognized under IFRS 15 due to the completion of development activities related to revenues associated with multiple collaborations in the year ended December 31, 2021. The increase was also driven by an increase of $4.3 million in grant revenue in the Controlled Founded Entities segment for the year ended December 31, 2021, which was driven primarily by Vedanta's grant revenue earned pursuant to its CARB-X and BARDA agreements. The aforementioned increases were partially offset by the a non-recurrent milestone payment of $2.0 million received from Karuna (and included in Parent Company and Other) in the year ended December 31, 2020.

Research and Development Expenses

	Year Ended December 31,		
(in thousands)	**2021**	2020	Change
Research and Development Expenses:			
Internal Segment	**$(65,444)**	$(45,346)	$20,098
Controlled Founded Entities	**(43,783)**	(36,279)	7,504
Non-Controlled Founded Entities	**—**	—	—
Parent Company and other	**(1,244)**	(234)	1,010
Total Research and Development Expenses:	**$(110,471)**	$(81,859)	$28,612

Our research and development expenses were $110.5 million for the year ended December 31, 2021, an increase of $28.6 million, or 35.0 percent compared to the year ended December 31, 2020. The change was primarily attributable to an increase of $20.1 million in research and development expenses incurred by the Internal segment due to the advancement of programs in clinical testing. This was primarily driven by an increase in clinical trial and clinical research organization expenditures of $14.0 million, an increase in research and development related consulting and professional fees of $2.5 million and an increase in research and development related salaries and stock compensation of $2.6 million. We progressed our ongoing clinical trials of LYT-100 and LYT- 200 in multiple indications and initiated clinical trials with respect to LYT 300, as well as advanced pre-clinical studies and research related to multiple candidates and research platforms. The increase was further attributable to an increase of $7.5 million in research and development expenses incurred by the Controlled Founded Entities segment, primarily attributable to Vedanta as they progressed their therapeutic candidates VE202, VE303, VE416 and VE800 towards meaningful milestones.

General and Administrative Expenses

	Year Ended December 31,		
(in thousands)	**2021**	2020	Change
General and Administrative Expenses:			
Internal Segment	**$(8,673)**	$(3,482)	$5,191
Controlled Founded Entities	**(20,729)**	(13,691)	7,038
Non-Controlled Founded Entities	**—**	—	—
Parent Company and other	**(27,797)**	(32,267)	(4,470)
Total General and Administrative Expenses	**$(57,199)**	$(49,440)	$7,760

Our general and administrative expenses were $57.2 million for the year ended December 31, 2021, an increase of $7.8 million, or 15.7 percent compared to the year ended December 31, 2020. The increase was primarily attributable to an increase of $7.0 million in the Controlled Founded Entities segment, which was primarily driven by non-cash increases of $2.9 million in stock based compensation expense, $1.4 million increase in payroll-related costs due to increased personnel, an increase in professional fees of $1.1 million, and an increase in legal fees of $0.9 million. The increase was further attributable to an increase of $5.2 million in the Internal segment, which was primarily driven by an increase in the management fee charged by the Parent company of $6.2 million which was partially offset by a decrease in depreciation expense of $0.5 million for the year ended December 31, 2021. The decrease in the Parent Company and other of $4.5 million was primarily attributable to the allocation of management fee charged to other segments of $7.0 million which was partially offset by an increase in professional and recruiting fees of $0.9 million and an increase in business insurance of $1.7 million for the year ended December 31, 2021.

Total Other Income (Loss)

Total other income was $160.0 million for the year ended December 31, 2021, a decrease of $18.7 million, compared to the year ended December 31, 2020. The decline in other income was primarily attributable to a decrease in gains from investments held at fair value of $53.4 million, primarily driven by the change in the fair value of the investment in Karuna. These gains from investments held at fair value were partially offset by losses realized on sale of certain investments held at fair value, as a result of the block sale discount included in the sale. The losses realized on sale of certain investments held at fair value for the year ended December 31, 2021 decreased $34.1 million compared to the year ended December 31, 2020.

Net Finance Income (Costs)

Net finance Income was $5.0 million for the year ended December 31, 2021, a change of $11.2 million, compared to net finance cost of $6.1 million for the year ended December 31, 2020. The change was primarily attributable to a $14.0 million change leading to increased income in respect of the change in the fair value of our preferred shares, warrant and convertible note liabilities held by third parties, partially offset by a $1.8 million increase in contractual finance costs, mainly in our controlled founded entity, Vedanta, and a $1.0 million decline in interest income from financial assets for the year ended December 31, 2021.

Share of Net Gain (Loss) in Associates Accounted for Using the Equity Method

For the year ended December 31, 2021, the share in net loss of associates reported under the equity method was $73.7 million as compared to the share of net loss of $34.1 million for the year ended December 31, 2020. The change was primarily attributable to an increase in Gelesis losses reported under IFRS for the year ended December 31, 2021 as compared to the losses reported for the year ended December 31, 2020, due to an increase in the fair value of Gelesis financial instrument liabilities that are accounted for at Fair Value Through Profit and Loss (FVTPL).

Taxation

Income tax expense was $3.8 million for the year ended December 31, 2021, as compared to income tax expense of $14.4 million for the year ended December 31, 2020. The decrease in income tax expense was primarily attributable to the decrease in profit before tax in entities in the U.S. Federal and Massachusetts consolidated return groups of the Company. For information on the change in the tax rate, see Note 25 in the consolidated financial statements.

Comparison of the Years Ended December 31, 2020 and 2019

Total Revenue

	Year Ended December 31,		
(in thousands)	2020	2019	Change
Contract Revenue:			
Internal Segment	$5,297	$7,077	$(1,780)
Controlled Founded Entities	990	1,474	(484)
Non-Controlled Founded Entities	—	—	—
Parent Company and other	2,054	137	1,917
Total Contract Revenue	$8,341	$8,688	$(347)
Grant Revenue:			
Internal Segment	$1,563	$928	$635
Controlled Founded Entities	1,864	191	1,673
Non-Controlled Founded Entities	—	—	—
Parent Company and other	—	—	—
Total Grant Revenue	$3,427	$1,119	$2,308
Total Revenue	$11,768	$9,807	$1,961

Our total revenue was $11.8 million for the year ended December 31, 2020, an increase of $2.0 million, or 20.0 percent compared to the year ended December 31, 2019. The increase was primarily attributable to an increase of $2.3 million in grant revenue in the Controlled Founded Entities segment for the year ended December 31, 2020, which was driven primarily by Vedanta's grant revenue earned pursuant to its CARB-X and BARDA agreements. The increase was further attributable to an increase of $1.9 million in contract revenue in the Parent segment for the year ended December 31, 2020, which was primarily driven by a $2.0 million milestone payment received from Karuna for initiation of its KarXT Phase 3 clinical study pursuant to the Exclusive Patent License Agreement between PureTech and Karuna. The increases were partially offset by a decline of $1.8 million in contract revenue in the Internal segment, which was primarily drive by the Orasome collaboration and license agreement with Roche, which concluded during the year ended December 31, 2020.

Research and Development Expenses

	Year Ended December 31,		
(in thousands)	2020	2019	Change
Research and Development Expenses:			
Internal Segment	$(45,346)	$(28,874)	$16,472
Controlled Founded Entities	(36,279)	(39,883)	(3,603)
Non-Controlled Founded Entities	—	(15,555)	(15,555)
Parent Company and other	(234)	(1,536)	(1,302)
Total Research and Development Expenses:	$(81,859)	$(85,848)	$(3,988)

Our research and development expenses were $81.9 million for the year ended December 31, 2020, a decline of $4.0 million, or 4.6 percent compared to the year ended December 31, 2019. The change was attributable to a decline of $15.6 million in the Non-Controlled Founded Entities segment owing to the deconsolidation of Vor, Karuna and Gelesis during year ended December 31, 2019. The decline was further attributable to declines of $3.6 million in the Controlled Founded Entities segment and $1.3 million in the Parent segment for the year ended December 31, 2020. The declines were partially offset by an increase of $16.5 million in research and development expenses incurred by the Internal segment for the year ended December 31, 2020. In 2020 we progressed our wholly-owned therapeutic candidates to key milestones. We completed a Phase 1 multiple ascending dose and food effect study for LYT-100. We also initiated a Phase 2a proof-of-concept study of LYT-100 in patients with breast cancer-related, upper limb secondary lymphedema as well as initiated a Phase 2 trial of LYT-100 in Long COVID respiratory complications and related sequelae, which is also known as post-acute COVID-19 syndrome (PACS). Finally, we initiated a Phase 1 clinical trial of LYT-200 for the potential treatment of metastatic solid tumors that are difficult to treat and have poor survival rates.

General and Administrative Expenses

(in thousands)	Year Ended December 31, 2020	2019	Change
General and Administrative Expenses:			
Internal Segment	$(3,482)	$(3,252)	$230
Controlled Founded Entities	(13,691)	(13,569)	122
Non-Controlled Founded Entities	—	(10,439)	(10,439)
Parent Company and other	(32,267)	(32,098)	168
Total General and Administrative Expenses	$(49,440)	$(59,358)	$(9,918)

Our general and administrative expenses were $49.4 million for the year ended December 31, 2020, a decrease of $9.9 million, or 16.7 percent compared to the year ended December 31, 2019. The decrease was primarily attributable to a decline of $10.4 million in the Non-Controlled Founded Entities segment, owing to the deconsolidation of Vor, Karuna and Gelesis during the year ended December 31, 2019.

Total Other Income (Loss)

Total other income was $178.7 million for the year ended December 31, 2020 a decrease of $493.4 million, compared to the year ended December 31, 2019. We recognized a gain on loss of significant influence of $445.6 million with respect to Karuna for the year ended December 31, 2019. No loss of significant influence of associates occurred during the year ended December 31, 2020. The decline was further attributable to a decline of $264.4 million in gain on deconsolidation as no deconsolidation of subsidiaries occurred during the year ended December 31, 2020, as compared to a gain of $264.4 million recognized for the deconsolidation of Vor, Karuna and Gelesis during the year ended December 31, 2019. The decline was further attributable to a loss of $55.0 million realized on the sale of certain investments held at fair value during year ended December 31, 2020. The declines were partially offset by an increase of $270.5 million on gain on investments held at fair value for the year ended December 31, 2020, which was primarily driven by Karuna.

Net Finance Income (Costs)

Net finance costs were $6.1 million for the year ended December 31, 2020, a decline of $40.0 million, or 86.7 percent compared to net finance costs of $46.1 million for the year ended December 31, 2019. The change was primarily attributable to a $42.1 million decline in the change in the fair value of our preferred shares, warrant and convertible note liabilities held by third parties for the year ended December 31, 2020.

Share of Net Gain (Loss) in Associates Accounted for Using the Equity Method, and Impairment of Investment in Associate

The share of net loss in associates was $34.1 million for the year ended December 31, 2020, a decrease of $64.9 million, or 210.8 percent as compared to net gain of $30.8 million for the year ended December 31, 2019. The change in share of net gain/(loss) in associates was primarily attributable to the financial results of Gelesis for the year ended December 31, 2020. Additionally, we allocated a share of our net loss in Gelesis for the year ended December 31, 2020, totaling $23.0 million, to our long-term interest in Gelesis as of December 31, 2020. We recorded equity method income of $37.1 million with respect to Gelesis, which was partially offset by our share of net loss in Karuna of $6.3 million for the year ended December 31, 2019. Additionally, we recorded an impairment charge of $42.9 million for the year ended December 31, 2019, related to our investment in common shares held in Gelesis. See Note 6 to our consolidated financial statements included elsewhere in this annual report.

Taxation

Income tax expense was $14.4 million for the year ended December 31, 2020, a decline of $98.0 million, or 87.2 percent as compared to the year ended December 31, 2019. The decline in income tax expense was primarily attributable to the gains realized on the loss of significant influence on Karuna for the year ended December 31, 2019 and the gains recognized on deconsolidation of Vor, Karuna and Gelesis during the year ended December 31, 2019.

Critical Accounting Policies and Significant Judgments and Estimates

Our management's discussion and analysis of our financial condition and results of operations is based on our financial statements, which we have prepared in accordance with international accounting standards in conformity with the requirements of the Companies Act 2006 and International Financial Reporting Standards (IFRSs) as adopted for use in the UK. The Consolidated Financial Statements also comply fully with IFRS as issued by the International Accounting Standards Board (IASB). In the preparation of these financial statements, we are required to make judgments, estimates and assumptions about the carrying amounts of assets and liabilities that are not readily apparent from other sources. The estimates and associated assumptions are based on historical experience and other factors that are considered to be relevant. Actual results may differ from these estimates under different assumptions or conditions.

Our estimates and assumptions are reviewed on an ongoing basis. Revisions to accounting estimates are recognized in the period in which the estimate is revised if the revision affects only that period or in the period of the revisions and future periods if the revision affects both current and future periods.

While our significant accounting policies are described in more detail in the notes to our consolidated financial statements appearing at the end of this report, we believe the following accounting policies to be most critical to the judgments and estimates used in the preparation of our financial statements. See Note 1 to our consolidated financial statements for a further detailed description of our significant accounting policies.

Financial instruments

We account for our financial instruments according to IFRS 9. As such, when issuing preferred shares in our subsidiaries we determine the classification of financial instruments in terms of liability or equity. Such determination involves significant judgement. These judgements include an assessment of whether the financial instruments include any embedded derivative features, whether they include contractual obligations upon us to deliver cash or other financial assets or to exchange financial assets or financial liabilities with another party at any point in the future prior to liquidation, and whether that obligation will be settled by exchanging a fixed amount of cash or other financial assets for a fixed number of the Group's equity instruments.

In accordance with IFRS 9 we carry certain investments in equity securities at fair value as well as our subsidiary preferred share, convertible notes and warrant liabilities, all through profit and loss (FVTPL). Valuation of the aforementioned financial instruments (assets and liabilities) includes making significant estimates, specifically determining the appropriate valuation methodology and making certain estimates of the future earnings potential of the subsidiary businesses, appropriate discount rate and earnings multiple to be applied, marketability and other industry and company specific risk factors.

Consolidation:

The consolidated financial statements include the financial statements of the Company and the entities it controls. Based on the applicable accounting rules, the Company controls an investee when it is exposed, or has rights, to variable returns from its involvement with the investee and has the ability to affect those returns through its power over the investee. Therefore an assessment is required to determine whether the Company has (i) power over the investee; (ii) exposure, or rights, to variable returns from its involvement with the investee; and (iii) the ability to use its power over the investee to affect the amount of the investor's returns. Judgement is required to perform such assessment and it requires that the Company considers, among others, activities that most significantly affect the returns of the investee, its voting shares, representation on the board, rights to appoint board members and management, shareholders agreements, de facto power, investee dependence on the Company and other contributing factors.

Investment in Associates

When we do not control an investee but maintain significant influence over the financial and operating policies of the investee the investee is an associate. Significant influence is presumed to exist when we hold 20 percent or more of the voting power of an entity, unless it can be clearly demonstrated that this is not the case. We evaluate if we maintain significant influence over associates by assessing if we have the power to participate in the financial and operating policy decisions of the associate.

Associates are accounted for using the equity method (equity accounted investees) and are initially recognized at cost, or if recognized upon deconsolidation they are initially recorded at fair value at the date of deconsolidation. The consolidated financial statements include our share of the total comprehensive income and equity movements of equity accounted investees, from the date that significant influence commences until the date that significant influence ceases. When our share of losses exceeds the net investment in an equity accounted investee, including preferred share investments that are considered to be Long-Term Interests, the carrying amount is reduced to zero and recognition of further losses is discontinued except to the extent that we have incurred legal or constructive obligations or made payments on behalf of an investee. To the extent we hold interests in associates that are not providing access to returns underlying ownership interests, the instrument held by PureTech is accounted for in accordance with IFRS 9.

Judgement is required in order to determine whether we have significant influence over financial and operating policies of investees. This judgement includes, among others, an assessment whether we have representation on the Board of Directors of the investee, whether we participate in the policy making processes of the investee, whether there is any interchange of managerial personnel, whether there is any essential technical information provided to the investee and if there are any transactions between us and the investee.

Judgement is also required to determine which instruments we hold in the investee form part of the investment in the associate, which is accounted for under IAS 28 and scoped out of IFRS 9, and which instruments are separate financial instruments that fall under the scope of IFRS 9. This judgement includes an assessment of the characteristics of the financial instrument of the investee held by us and whether such financial instrument provides access to returns underlying an ownership interest.

Where the company has other investments in an equity accounted investee that are not accounted for under IAS 28, judgement is required in determining if such investments constitute Long-Term Interests for the purposes of IAS 28 (please refer to Notes 5 and 6). This determination is based on the individual facts and circumstances and characteristics of each investment, but is driven, among other factors, by the intention and likelihood to settle the instrument through redemption or repayment in the foreseeable future, and whether or not the investment is likely to be converted to common stock or other equity instruments

Recent Accounting Pronouncements

For information on recent accounting pronouncements, see our consolidated financial statements and the related notes found elsewhere in this report.

Cash Flow and Liquidity

Our cash flows may fluctuate and are difficult to forecast and will depend on many factors, including:

- the expenses incurred in the development of wholly-owned and Controlled Founded Entity therapeutic candidates;
- the revenue, if any, generated by wholly-owned and Controlled-Founded Entity therapeutic candidates;
- the revenue, if any, generated from licensing and royalty agreement with Founded Entities;
- the financing requirements of the Internal segment, Controlled-Founded Entities segment and Parent segment; and
- the investment activities in the Internal, Controlled-Founded Entities, and Non-Controlled Founded Entities and Parent segments.

As of December 31, 2021, we had consolidated cash and cash equivalents of $465.7 million. As of December 31, 2021, we had PureTech Level cash and cash equivalents of $418.9 million (for a definition of PureTech Level cash and cash equivalents, see paragraph "Cash flow and cash equivalents" earlier in this Financial review).

Cash Flows

The following table summarizes our cash flows for each of the periods presented:

	Year Ended December 31,		
(in thousands)	**2021**	2020	2019
Net cash used in operating activities	**$(158,274)**	$(131,827)	$(98,156)
Net cash provided by investing activities	**197,375**	364,478	63,659
Net cash provided by financing activities	**22,727**	38,869	49,910
Effect of exchange rates on cash and cash equivalents	**—**	—	(104)
Net increase in cash and cash equivalents	**$61,827**	$271,520	$15,309

Operating Activities

Net cash used in operating activities was $158.3 million for the year ended December 31, 2021, as compared to $131.8 million for the year ended December 31, 2020. The increase in outflows is primarily attributable to our higher operating loss and higher income taxes paid of $7.0 million, and to a lesser extent the timing of receipts and payments in the normal course of business.

Net cash used in operating activities was $131.8 million for the year ended December 31, 2020, as compared to $98.2 million for the year ended December 31, 2019. The increase in outflows was primarily attributable to estimated income taxes of $20.7 million paid for our disposals of Karuna common shares during the year ended December 31, 2020. The increase was further attributable to a decrease of $4.5 million in payments received with respect to contract revenue for the year ended December 31, 2020. We received a $2.0 million milestone payment from Karuna for initiation of its KarXT Phase 3 clinical study pursuant to the Exclusive Patent License Agreement between PureTech and Karuna during the year ended December 31, 2020. We received $3.5 million from Imbrium Therapeutics LP for the execution of a Research Collaboration Option and License Agreement and $3.0 million from Boehringer Ingelheim for the execution of a Collaboration and License Agreement during the year ended December 31, 2019. The increase in outflows was further attributable to reduced interest income and the timing of payments in the normal course of business for the year ended December 31, 2020.

Investing Activities

Net cash provided by investing activities was $197.4 million for the year ended December 31, 2021, as compared to inflows of $364.5 million for the year ended December 31, 2020, resulting in a decrease of $167.1 million in net cash provided by investing activities. The decrease in the net cash provided by investing activities was primarily attributed to the decrease in proceeds from the sale of investments held at fair value of $132.5 million (proceeds from such sales were $218.1 million for the year ended December 31, 2021 vs. $350.6 million for the year ended December 30, 2020) and the fact that for the year ended December 31, 2020 the Company had proceeds of $30.1 million from maturity of short term investments while for the year ended December 31, 2021, there were no such cash inflows.

Net cash provided by investing activities was $364.5 million for the year ended December 31, 2020, as compared to inflows of $63.7 million for the year ended December 31, 2019. The inflow was primarily attributable to the sale of Karuna and resTORbio common shares for aggregate proceeds of $350.6 million during the year ended December 31, 2020. The inflow was further attributable to cash provided by the maturity of short-term investments totaling $30.1 million. The inflows were offset by purchases of Gelesis and Vor preferred shares totaling $11.1 million and the purchase of fixed assets totaling $5.2 million.

Financing Activities

Net cash provided by financing activities was $22.7 million for the year ended December 31, 2021, as compared to $38.9 million for the year ended December 31, 2020, resulting in a decrease of $16.1 million in the net cash provided by financing activities. The decrease in the net cash provided by financing activities was primarily attributable to the decrease in proceeds from issuance of convertible notes in subsidiaries of $22.8 million and the fact that for the year ended December 31, 2020 the Company had proceeds from the issuance of a long term loan of $14.7 million, while for the year ended December 31, 2021, there was no such cash inflow. Such decreases were partially offset by an increase in proceeds from issuance of preferred shares in subsidiaries of $23.9 million

Net cash provided by financing activities was $38.9 million for the year ended December 31, 2020, as compared to $49.9 million for the year ended December 31, 2019. The net inflow was primarily attributable to the issuances by Vedanta of a $25.0 million convertible promissory note and a long-term loan with net proceeds of $14.7 million. The inflow was further attributable to $13.8 million received from the Vedanta Series C-2 and Sonde Series A-2 preferred share financings. The inflows were partially offset by the $12.9 million settlement of 2017 RSU awards granted to certain executives.

Funding Requirements

We have incurred operating losses since inception. Based on our current plans, we believe our existing cash and cash equivalents at December 31, 2021, will be sufficient to fund our operations and capital expenditure requirements into the first quarter of 2025. We expect to incur substantial additional expenditures in the near term to support our ongoing activities. We anticipate to continue to incur net operating losses for the foreseeable future as is typical for pre-revenue biotechnology companies. Our ability to fund our therapeutic development and clinical operations as well as commercialization of our wholly-owned therapeutic candidates, will depend on the amount and timing of cash received from planned financings and potential business development activities. Our future capital requirements will depend on many factors, including:

- the costs, timing and outcomes of clinical trials and regulatory reviews associated with our wholly-owned therapeutic candidates;
- the costs of commercialization activities, including product marketing, sales and distribution;
- the costs of preparing, filing and prosecuting patent applications and maintaining, enforcing and defending intellectual property-related claims;
- the emergence of competing technologies and products and other adverse marketing developments;
- the effect on our therapeutic and product development activities of actions taken by the U.S. Food and Drug Administration ("FDA"), the European Medicines Agency ("EMA") or other regulatory authorities;
- our degree of success in commercializing our wholly-owned therapeutic candidates, if and when approved; and
- the number and types of future therapeutics we develop and commercialize.

A change in the outcome of any of these or other variables with respect to the development of any of our wholly-owned therapeutic candidates could significantly change the costs and timing associated with the development of that therapeutic candidate.

Further, our operating plans may change, and we may need additional funds to meet operational needs and capital requirements for clinical trials and other research and development activities. We currently have no credit facility or other committed sources of capital. Because of the numerous risks and uncertainties associated with the development and commercialization of our wholly-owned therapeutic candidates, we have only a general estimate of the amounts of increased capital outlays and operating expenditures associated with our current and anticipated therapeutic development programs and these may change in the future.

Financial Position

Summary Financial Position

	As of December 31,		
(in thousands)	**2021**	2020	Change
Investments held at fair value (*)	**397,179**	530,161	(132,982)
Other non-current assets	**47,018**	45,484	1,534
Non-current assets	**444,197**	575,645	(131,448)
Cash and cash equivalents	**465,708**	403,881	61,827
Other current assets	**36,101**	10,468	25,634
Current assets	**501,809**	414,348	87,461
Total assets	**946,006**	989,994	(43,988)
Lease Liability	**29,040**	32,088	(3,048)
Deferred tax liability	**89,765**	108,626	(18,861)
Other non-current liabilities	**16,921**	14,818	2,103
Non-current liabilities	**135,725**	155,531	(19,806)
Trade and other payables	**35,760**	20,566	15,194
Notes payable	**3,916**	26,455	(22,539)
Warrant liability	**6,787**	8,206	(1,419)
Preferred shares	**174,017**	118,972	55,045
Other current liabilities	**5,654**	6,724	(1,069)
Current liabilities	**226,135**	180,924	45,211
Total liabilities	**361,859**	336,455	25,405
Net assets	**584,147**	653,539	(69,392)
Total equity	**584,147**	653,539	(69,392)

(*) Fair value of investments accounted for at fair value, does not take into consideration contribution from milestones that occurred after December 31, 2021, the value of our consolidated Founded Entities (Vedanta, Follica, Sonde, Alivio, and Entrega), our Wholly Owned Programs, or our cash.

Investments Held at Fair Value

Investments held at fair value decreased $133.0 million to $397.2 million as of December 31, 2021. Investments held at fair value consists primarily of our common share investment in Karuna and Vor (from February 2021) and our preferred share investments in Akili, Gelesis and Vor (until February 2021). See Note 5 to our consolidated financial statements included elsewhere in this annual report for details regarding the change in investments held at fair value.

Cash and Cash Equivalents

Consolidated cash, cash equivalents increased $61.8 million to $465.7 million as of December 31, 2021, while we had PureTech Level cash and cash equivalents of $418.9 million. The increase reflected primarily the disposals of Karuna common shares during the year ended December 31, 2021. On February 9, 2021, PureTech sold 1,000,000 shares of Karuna common shares for aggregate proceeds of $118.0 million. On November 9, 2021, PureTech sold an additional 750,000 Karuna common shares for aggregate proceeds of $100.1 million. The inflows from the disposals were primarily offset by our operating loss of $150.3 million for the year ended December 31, 2021.

Non-Current Liabilities

Non-current liabilities decreased $19.8 million to $135.7 million as of December 31, 2021. The decrease was driven by declines of $3.0 million and $18.9 million in our long-term lease and deferred tax liabilities, respectively as of December 31, 2021.

Trade and Other Payables

Trade and other payables increased $15.2 million to $35.8 million as of December 31, 2021. The increase reflected primarily the timing of payments as of December 31, 2021.

Notes Payable

Notes payable decreased $22.5 million to $3.9 million as of December 31, 2021. The decrease reflected the conversion of the Vedanta $25.0 million convertible promissory note to a third party investor during the execution of the Series D financing round. This decrease was partially offset by a $2.2 million note issuance by Sonde.

Preferred Shares

Preferred share liability increased $55.0 million to $174.0 million as of December 31, 2021. The increase reflected the issuance by Vedanta of Series D preferred shares and the conversion of Vedanta notes into Series D preferred shares, increasing the liability by $63.4 million. This increases was partially offset by a decrease in fair value of the preferred share liability by $8.4 million during the year ended December 31, 2021.

Quantitative and Qualitative Disclosures about Financial Risks

Interest Rate Sensitivity

As of December 31, 2021, we had consolidated cash and cash equivalents of $465.7 million, while we had PureTech Level cash and cash equivalents of $418.9 million. Our exposure to interest rate sensitivity is impacted by changes in the underlying U.K. and U.S. bank interest rates. We have not entered into investments for trading or speculative purposes. Due to the conservative nature of our investment portfolio, which is predicated on capital preservation and investments in short duration, high-quality U.S. Treasury Bills and U.S. debt obligations and related money market accounts we do not believe change in interest rates would have a material effect on the fair market value of our portfolio, and therefore we do not expect our operating results or cash flows to be significantly affected by changes in market interest rates.

Foreign Currency Exchange Risk

We maintain our consolidated financial statements in our functional currency, which is the U.S. dollar. Monetary assets and liabilities denominated in currencies other than the functional currency are translated into the functional currency at rates of exchange prevailing at the balance sheet dates. Non-monetary assets and liabilities denominated in foreign currencies are translated into the functional currency at the exchange rates prevailing at the date of the transaction. Exchange gains or losses arising from foreign currency transactions are included in the determination of net income (loss) for the respective periods. Such foreign currency gains or losses were not material for all reported periods.

We recorded foreign currency losses in respect of foreign operations of $0.0 million, $0.5 million and $0.0 million for the years ended December 31, 2021, December 31, 2020, and December 31, 2019, respectively, which are included in Other comprehensive income/(loss) in the Consolidated Statements of Comprehensive Income/(Loss).

We do not currently engage in currency hedging activities in order to reduce our currency exposure, but we may begin to do so in the future. Instruments that may be used to hedge future risks include foreign currency forward and swap contracts. These instruments may be used to selectively manage risks, but there can be no assurance that we will be fully protected against material foreign currency fluctuations.

Controlled Founded Entity Investments

We maintain investments in certain Controlled Founded Entities. Our investments in Controlled Founded Entities are eliminated as intercompany transactions upon financial consolidation. We are however exposed to a preferred share liability owing to the terms of existing preferred shares and the ownership of Controlled Founded Entities preferred shares by third parties. The liability of preferred shares is maintained at fair value through the profit and loss. Our strong cash position, budgeting and forecasting processes, as well as decision making and risk mitigation framework enable us to robustly monitor and support the business activities of the Controlled Founded Entities to ensure no exposure to credit losses and ultimately dissolution or liquidation. Accordingly, we view exposure to third party preferred share liability as low. Please refer to Note 16 to our consolidated financial statements for further information regarding our exposure to Controlled Founded Entity Investments.

Non-Controlled Founded Entity Investments

We maintain certain investments in Non-Controlled Founded Entities which are deemed either as investments and accounted for as investments held at fair value or associates and accounted for under the equity method (please refer to Note 1 to our consolidated financial statements). Our exposure to investments held at fair value was $397.2 million as of December 31, 2021, and we may or may not be able to realize the value in the future. Accordingly, we view the risk as high. Our exposure to investments in associates in limited to the carrying amount of the investment. We are not exposed to further contractual obligations or contingent liabilities beyond the value of initial investment. As of December 31, 2021, Gelesis was the only associate. The carrying amount of the investment in Gelesis as an associate was zero. Accordingly, we do not view this as a risk. Please refer to Notes 5, 6 and 16 to our consolidated financial statements for further information regarding our exposure to Non-Controlled Founded Entity Investments.

Equity Price Risk

As of December 31, 2021, we held 1,656,564 common shares of Karuna and 3,207,200 common shares of Vor. The fair value of our investment in the common shares of Karuna was $217.0 million and common shares of Vor was $37.3 million.

The investments in Karuna and Vor are exposed to fluctuations in the market price of these common shares. The effect of a 10.0 percent adverse change in the market price of Karuna common shares and Vor common shares as of December 31, 2021, would have been a loss of approximately $21.7 million and $3.7 million, respectively, recognized as a component of Other income (expense) in our Consolidated Statements of Comprehensive Income/(Loss).

Subsequent to December 31, 2021 our investment in Gelesis was converted into shares of common stock of Gelesis (after the combination with Capstar), which are publicly traded on the New York Stock Exchange.

Liquidity Risk

We do not believe we will encounter difficulty in meeting the obligations associated with our financial liabilities that are settled by delivering cash or another financial asset. While we believe our cash and cash equivalents do not contain excessive risk, we cannot provide absolute assurance that in the future our investments will not be subject to adverse changes or decline in value based on market conditions.

Credit Risk

We maintain an investment portfolio in accordance with our investment policy. The primary objectives of our investment policy are to preserve principal, maintain proper liquidity and to meet operating needs. Although our investments are subject to credit risk, our investment policy specifies credit quality standards for our investments and limits the amount of credit exposure from any single issue, issuer or type of investment. Also, due to the conservative nature of our investments and relatively short duration, interest rate risk is mitigated. We do not own derivative financial instruments. Accordingly, we do not believe that there is any material market risk exposure with respect to derivative or other financial instruments.

Credit risk is also the risk of financial loss if a customer or counterparty to a financial instrument fails to meet its contractual obligations. We assess the credit quality of customers on an ongoing basis, taking into account its financial position, past experience and other factors. The credit quality of financial assets that are neither past due nor impaired can be assessed by reference to credit ratings (if available) or to historical information about counterparty default rates. We are also potentially subject to concentrations of credit risk in accounts receivable. Concentrations of credit risk with respect to receivables is owed to the limited number of companies comprising our customer base. However, our exposure to credit losses is currently de minimis due to the credit quality of our receivables, which are primarily from the US government and large funds with respect to grants.

Foreign Private Issuer Status

Owing to our U.S. listing, we report under the Securities Exchange Act of 1934, as amended, or the Exchange Act, as a non-U.S. company with foreign private issuer status. As long as we qualify as a foreign private issuer under the Exchange Act, we will be exempt from certain provisions of the Exchange Act that are applicable to U.S. domestic public companies, including:

- the sections of the Exchange Act regulating the solicitation of proxies, consents or authorizations in respect of a security registered under the Exchange Act;
- sections of the Exchange Act requiring insiders to file public reports of their stock ownership and trading activities and liability for insiders who profit from trades made in a short period of time;
- the rules under the Exchange Act requiring the filing with the SEC of quarterly reports on Form 10-Q containing unaudited financial and other specified information, or current reports on Form 8-K, upon the occurrence of specified significant events; and
- Regulation FD, which regulates selective disclosures of material information by issuers.

Chair's overview

"We believe that good corporate governance is essential for building a successful and sustainable business."

Dear Shareholder

I am pleased to introduce our Corporate Governance Report. This section sets out our governance framework and the work of the Board and its committees.

As a Board, we are responsible for ensuring there is an effective governance framework in place. This includes setting the Company's strategic objectives, ensuring the right leadership and resources are in place to achieve these objectives, monitoring performance, ensuring that sufficient internal controls and protections are in place and reporting to shareholders. An effective governance framework is also designed to ensure accountability, fairness and transparency in the Company's relationships with all of its stakeholders, whether shareholders, employees, partners, the government or the wider patient community. We believe that good corporate governance is essential for building a successful and sustainable business.

The Board is committed to the highest standards of corporate governance and undertakes to maintain a sound framework for our control and management. In this report, we provide details of that framework.

The key constituents necessary to deliver a robust structure are in place and, accordingly, this report includes a description of how the Company has applied the principles and provisions of the Governance Code and how it intends to apply those principles in the future.

The Board looks forward to being able to discuss these matters with our shareholders in connection with our AGM or indeed at any other time during the year.

Christopher Viehbacher
Chair

April 25, 2022

Board of Directors

(alphabetically)*

PureTech Health is led by a seasoned and accomplished Board of Directors and management team with extensive experience in maximising shareholder value, discovering scientific breakthroughs, and delivering therapeutics to market.

Sharon Barber-Lui
Independent Non-Executive Director

Sharon Barber-Lui has served as a member of our Board since March 2022. Ms. Barber-Lui has been the Senior Vice President of Finance at EQRx since January 2022. Prior to joining EQRx, Ms. Barber-Lui worked at Merck for over twenty years in roles of advancing responsibility, including most recently as the Head of Portfolio Market Strategy, Operations and Business Analytics from 2019 through 2021 and Chief Financial Officer from 2014 through 2018 for Merck's U.S. oncology business. Prior to that Ms. Barber-Lui held a number of other roles with Merck including Treasurer of U.S. Region, Head of U.S. Treasury Operations, and Head of Legal Entity Integration and Global Treasury Services, among others. Ms. Barber-Lui began her career as an accountant for KPMG LLP, and she received her bachelor's degree as well as her M.B.A. from Lehigh University. Ms. Barber-Lui is a member of the American Institute of Certified Public Accountants.

Raju Kucherlapati, Ph.D.
Independent Non-Executive Director, R&D Committee Member

Raju Kucherlapati, Ph.D., has served as a member of our Board since 2014. He has been the Paul C. Cabot professor of Genetics and a professor of medicine at Harvard Medical School since 2001. Dr. Kucherlapati currently serves on the board of directors of Gelesis, Inc. and KEW Inc. He was a founder and former board member of Abgenix, Cell Genesys and Millennium Pharmaceuticals. He is a fellow of the American Association for the Advancement of Science and a member of the National Academy of Medicine. Dr. Kucherlapati received his Ph.D. from the University of Illinois. He trained at Yale and has held faculty positions at Princeton University, University of Illinois College of Medicine and the Albert Einstein College of Medicine. He served on the editorial board of the New England Journal of Medicine and was Editor in Chief of the journal Genomics. His laboratory at Harvard Medical School is involved in cloning and characterization of human disease genes with a focus on human syndromes with a significant cardiovascular involvement, use of genetic/genomic approaches to understand the biology of cancer and the generation and characterization of genetically modified mouse models for cancer and other human disorders.

John LaMattina, Ph.D.
Independent Non-Executive Director, R&D Committee Member

John LaMattina, Ph.D., has served as a member of our Board since 2009. Dr. LaMattina previously worked at Pfizer in different roles from 1977 to 2007, including vice president of U.S. Discovery Operations in 1993, senior vice president of worldwide discovery operations in 1998, senior vice president of worldwide development in 1999 and president of global research and development from 2003 to 2007. Dr. LaMattina serves on the board of directors of Ligand Pharmaceuticals, Immunome Inc. and Vedanta. Dr. LaMattina previously served on the board of Zafgen, Inc. until April 2020. He also serves on the Scientific Advisory Board of Frequency Therapeutics and is a trustee associate of Boston College. During Dr. LaMattina's leadership tenure, Pfizer discovered and/or developed a number of important new medicines including Tarceva, Chantix, Zoloft, Selzentry and Lyrica, along with a number of other medicines currently in late stage development for cancer, rheumatoid arthritis and pain. He is the author of numerous scientific publications and U.S. patents. Dr. LaMattina received the 1998 Boston College Alumni Award of Excellence in Science and the 2004 American Diabetes Association Award for Leadership and Commitment in the Fight Against Diabetes. He was awarded an Honorary Doctor of Science degree from the University of New Hampshire in 2007. In 2010, he was the recipient of the American Chemical Society's Earle B. Barnes Award for Leadership in Chemical Research Management. He is the author of *"Devalued and Distrusted—Can the Pharmaceutical Industry Restore its Broken Image," "Drug Truths: Dispelling the Myths About Pharma R&D"* and an author of the Drug Truths blog at Forbes.com. Dr. LaMattina received a B.S. in Chemistry from Boston College and received a Ph.D. in Organic Chemistry from the University of New Hampshire. He then moved on to Princeton University as a National Institutes of Health postdoctoral fellow in the laboratory of professor E. C. Taylor.

* Biographies for executive directors, Daphne Zohar and Bharatt Chowrira, can be found on pages 115 to 116.

Robert Langer, Sc.D.
Co-Founder and Non-Executive Director, R&D Committee Member

Robert S. Langer, Sc.D., has served as a member of our Board since our founding and is our co-founder. Dr. Langer has served as the David H. Koch Institute professor at MIT since 2005. He served as a member of the FDA's science board from 1995 to 2002 and as its chairman from 1999 to 2002. Dr. Langer serves on the board of directors of Seer Bio, Abpro Bio, Frequency Therapeutics, Entrega, Inc. and Moderna, Inc. Dr. Langer has received over 220 major awards, including the 2006 U.S. National Medal of Science, the Charles Stark Draper Prize in 2002 and the 2012 Priestley Medal. He is also the first engineer to ever receive the Gairdner Foundation International Award. Dr. Langer has received the Dickson Prize for Science, Heinz Award, Harvey Prize, John Fritz Award, General Motors Kettering Prize for Cancer Research, Dan David Prize in Materials Science, Breakthough Prize in Life Sciences, National Medal of Science, National Medal of Technology and Innovation, Kyoto Prize, Wolf Prize, Albany Medical Center Prize in Medicine and Biomedical Research and the Lemelson-MIT prize. In 2006, he was inducted into the National Inventors Hall of Fame. In January 2015, Dr. Langer was awarded the 2015 Queen Elizabeth Prize for Engineering. Dr. Langer received his bachelor's degree in Chemical Engineering from Cornell University and his Sc.D. in Chemical Engineering from MIT.

Kiran Mazumdar-Shaw
Independent Non-Executive Director

Kiran Mazumdar-Shaw has served as a member of our Board since September 2020. Ms. Mazumdar-Shaw has been the executive chairperson of Biocon Limited, which she founded in 1978, since April 2020, and she served as managing director of Biocon Limited from 1995 to 2020. Ms. Mazumdar-Shaw holds key positions in various industry, educational, government and professional bodies globally. She has been elected as a full-term member of the board of trustees of Massachusetts Institute of Technology. She has been elected as a member of the prestigious U.S.-based National Academy of Engineering. She also serves as the lead independent member of the board of Infosys Ltd, a director on the board of United Breweries Limited, and non-executive director on the board of Narayana Health. Ms. Mazumdar-Shaw has received two of India's highest civilian honors, the Padma Shri in 1989 and the Padma Bhushan in 2005. She was also honored with the Order of Australia, Australia's highest civilian honor in January 2020. In 2016, she was conferred with the highest French distinction – Knight of the Legion of Honour – and in 2014 received the Othmer Gold Medal in 2014 from the U.S.-based Chemical Heritage Foundation for her pioneering efforts in biotechnology. Ms. Mazumdar-Shaw has been ranked as one of the world's top 20 inspirational leaders in the field of biopharmaceuticals by The Medicine Maker Power List 2020, and she was the winner of EY World Entrepreneur of the Year™ 2020 Award. She was the first woman business leader from India to sign the Giving Pledge, an initiative of the Gates Foundation, committing to give the majority of her wealth to philanthropic causes. She received a bachelor's degree in science, Zoology Hons., from Bangalore University and a master's degree in malting and brewing from Ballarat College, Melbourne University. She has been awarded several honorary degrees from other universities globally.

Dame Marjorie Scardino
Senior Independent Director

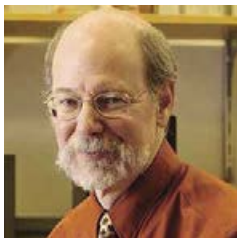
Dame Marjorie Scardino has served as a member of our Board since 2015. She served for 28 years as the chief executive officer of Pearson, a large education company that included The Economist, The Financial Times and Penguin Books. She was on the board of the MacArthur Foundation for 12 years, five as chairman, and left in 2017. She was a member of the board of Twitter from 2013 to 2018 and International Airlines Group from 2014 to 2019. Dame Scardino has received a number of honorary degrees, and in 2003 was dubbed a dame of the British Empire. She is also a member of the Royal Society of the Arts in the UK and the American Association of Arts and Sciences.

Christopher Viehbacher
Chair

Chris Viehbacher has served as a member of our Board since 2015 and as chairman since September 2019. He has been the managing partner of Gurnet Point Capital since October 2014. Immediately prior to joining Gurnet Point Capital, Mr. Viehbacher served as the chief executive officer and member of the board of directors of Sanofi from December 2008 to October 2014. From 1993 to 2008, Mr. Viehbacher worked at GlaxoSmithKline in different roles, including ultimately President of its North American pharmaceutical division. Mr. Viehbacher began his career with PricewaterhouseCoopers LLP and qualified as a chartered accountant. Mr. Viehbacher currently serves on the board of directors of Vedanta Biosciences as chairman, BEFORE Brands, Crossover Health, Boston Pharmaceuticals, Zikani and Gurnet Point Capital LLC. Mr. Viehbacher previously served on the board of directors of Axcella Health Inc. and Corium International, Inc. Mr. Viehbacher also serves on the Board of Trustees of Northeastern University and the Board of Fellows of Stanford Medical School. Mr. Viehbacher has co-chaired the Chief Executive Officer Roundtable on Neglected Diseases with Bill Gates and formerly chaired the chief executive officer Roundtable on Cancer. He was the chairman of the board of the Pharmaceutical Research and Manufacturers of America as well as president of the European Federation of Pharmaceutical Industries and Associations. At the World Economic Forum at Davos, Mr. Viehbacher was a chair of the Health Governors and co-chaired an initiative to create a Global Charter for Healthy Living. He was also a member of the International Business Council. Mr. Viehbacher has received the Pasteur Foundation Award for outstanding commitment to safeguarding and improving health worldwide. He has also received France's highest civilian honor, the Légion d'honneur. Mr. Viehbacher received his bachelor's degree in Commerce from Queen's University in Ontario, Canada in 1983.

Dennis Ausiello, M.D.**
Board Advisor, R&D Committee Member

Dennis Ausiello, M.D., is a board advisor and member of the PureTech R&D Committee. He is the Jackson Distinguished Professor of Clinical Medicine and was previously director, emeritus of the M.D./Ph.D. Program at Harvard Medical School. Dr. Ausiello is chairman of medicine, emeritus and director of the Center for Assessment Technology and Continuous Health (CATCH) at Massachusetts General Hospital (MGH). This center is a partnership among MGH, MIT and Harvard University with a mission to develop real-time assessment of human traits in wellness and disease. In partnership with industry, it is creating tools for measurements of traditional and novel phenotypes. Understanding the need for partnerships between the academy and industry, Dr. Ausiello served on the board of directors of Pfizer Pharmaceuticals, where he was their former lead director. He currently serves as a member of the board of directors of Seres Health and Alnylam. Dr. Ausiello is also a member of the board of directors of several non-public biotech companies and is a consultant to Verily (formerly Google Life Sciences) and Pfizer Pharmaceuticals. Dr. Ausiello is a nationally recognized leader in academic medicine who was elected to the National Academy of Medicine in 1999 and the American Academy of Arts and Sciences in 2003. He has published numerous articles, book chapters and textbooks and has served as an editor of Cecil's Textbook of Medicine. Dr. Ausiello received his BA from Harvard College and an M.D. from the University of Pennsylvania.



H. Robert Horvitz, Ph.D.**
Board Advisor, R&D Committee Chair

H. Robert Horvitz, Ph.D., is a board observer and Chair of the R&D Committee at PureTech. He received the Nobel Prize in Physiology or Medicine and is the David H Koch Professor of Biology at Massachusetts Institute of Technology, an investigator of the Howard Hughes Medical Institute, neurobiologist (Neurology) at Massachusetts General Hospital, a member of the MIT McGovern Institute for Brain Research and the MIT Koch Institute for Integrative Cancer Research. He is cofounder of multiple life science companies, including Epizyme (EPZM), Mitobridge (acquired by Astellas) and Idun Pharmaceuticals (acquired by Pfizer) and was a member of the Scientific Advisory Board of the Novartis Institutes for BioMedical Research.

Dr. Horvitz was a member of the board of trustees of the Massachusetts General Hospital. He also previously served as Chairman of the Board of Trustees of the Society for Science and the Public and as President of the Genetics Society of America. Dr. Horvitz is a member of the U.S. National Academy of Sciences, the U.S. National Academy of Medicine and the American Philosophical Society and is a foreign member of the Royal Society of London. He is a fellow of the American Academy of Arts and Sciences and of the American Academy of Microbiology.

Dr. Horvitz received the U.S. National Academies of Science Award in Molecular Biology; the Charles A. Dana Award for Pioneering Achievements in Health; the Ciba-Drew Award for Biomedical Science; the General Motors Cancer Research Foundation Alfred P. Sloan, Jr. Prize; the Gairdner Foundation International Award; the March of Dimes Prize in Developmental Biology; the Genetics Society of America Medal; the Bristol-Myers Squibb Award for Distinguished Achievement in Neuroscience; the Wiley Prize in the Biomedical Sciences; the Peter Gruber Foundation Genetics Prize; the American Cancer Society Medal of Honor; the Alfred G. Knudson Award of the National Cancer Institute; and the UK Genetics Society Mendel Medal. He has received honorary doctoral degrees from the University of Rome, Cambridge University, Pennsylvania State University and the University of Miami.

Bennett Shapiro, M.D.**
Board Advisor, R&D Committee Member

Bennett Shapiro, M.D., is a PureTech co-founder, a board advisor, a member of PureTech's R&D Committee. He also served as member of the Board from the Company's founding through June 2020. Dr. Shapiro was previously Executive Vice President at Merck Research Laboratories of Merck & Co. where he initially led Worldwide Basic Research and was responsible for all the basic and preclinical research activities at Merck. He later led Worldwide Licensing and External Research and was responsible for Merck's relationships with the academic and industrial biomedical research community. His leadership resulted in the discovery, development and registration of approximately 25 drugs and vaccines. Previously, he was professor and chairman of the Department of Biochemistry at the University of Washington and is the author of over 120 papers on the molecular regulation of cellular behavior. Following an internship in Medicine at the University of Pennsylvania Hospital, he was a Research Associate at the NIH, then a Visiting Scientist at the Institut Pasteur in Paris and returned to the NIH as Chief-Section on Cellular Differentiation in the Laboratory of Biochemistry prior to joining the University of Washington. Dr. Shapiro has been a Guggenheim Fellow, a Fellow of the Japan Society for the Promotion of Science and a Visiting Professor at the University of Nice. He currently serves as a member of the board of directors of Vedanta Biosciences and VBL Therapeutics. Dr. Shapiro previously served as a director of Celera Corporation, the Drugs for Neglected Diseases initiative and the Mind and Life Institute. Dr. Shapiro received a B.S. in Chemistry from Dickinson College and his M.D. from Jefferson Medical College.

** Dr. Horvitz, Dr. Ausiello and Dr. Shapiro are not members of the PureTech Board. As a Board Observer, Dr. Horvitz attends the majority of Board meetings. As Board Advisors, Dr. Ausiello and Dr. Shapiro attend select Board meetings. All three are also members of PureTech's R&D Committee, of which Dr. Horvitz is the Chair.

Management team

(alphabetically)

Joseph Bolen, Ph.D.
Chief Scientific Officer

Joseph Bolen, Ph.D., first joined PureTech in October 2015 and has served as PureTech's chief scientific officer since October 2016. Prior to joining PureTech, Dr. Bolen oversaw all aspects of research and development, or R&D, for Moderna, Inc. as president and chief scientific officer from July 2013 to October 2015. Previously, he was chief scientific officer and global head of oncology research at Millennium: The Takeda Oncology Company. Prior to joining Millennium in 1999, Dr. Bolen held senior positions at Hoechst Marion Roussel, Schering-Plough and Bristol-Myers Squibb. Dr. Bolen began his career at the National Institutes of Health, where he contributed to the discovery of a class of proteins known as tyrosine kinase oncogenes as key regulators of the immune system. Dr. Bolen received a B.S. in Microbiology & Chemistry and a Ph.D. in Immunology from the University of Nebraska and conducted his postdoctoral training in Molecular Virology at the Kansas State University Cancer Center.

Bharatt Chowrira, Ph.D., J.D.
President and Chief Business, Legal and Operating Officer, Member of the Board of Directors

Bharatt Chowrira, Ph.D., J.D., has been our president and chief business, legal and operating officer since January, 2022 and was our president and chief of business and strategy from March 2017 through December 2021. Dr. Chowrira has also served as a member of PureTech's Board since February 1, 2021. Prior to joining PureTech, Dr. Chowrira was the president of Synlogic, Inc., a biopharmaceutical company focused on developing synthetic microbiome-based therapeutics, from September 2015 to February 2017, where he oversaw and managed corporate and business development, alliance management, financial, human resources, intellectual property and legal operations. Prior to that, Dr. Chowrira was the chief operating officer of Auspex Pharmaceuticals, Inc. from October 2013 to July 2015, which was acquired by Teva Pharmaceuticals Ltd. in the spring of 2015. Previously, he was president and chief executive officer of Addex Therapeutics Ltd., a biotechnology company publicly-traded on the SIX Swiss Exchange, from August 2011 to July 2013. Prior to that Dr. Chowrira held various leadership and management positions at Nektar Therapeutics (chief operating officer), Merck & Co, or Merck (vice president), Sirna Therapeutics (general counsel; acquired by Merck) and Ribozyme Pharmaceuticals (chief patent counsel). Dr. Chowrira is currently a member of the board of directors of Vedanta Biosciences, Inc. and Akili Interactive Labs, Inc., and, he previously served on the board of directors of Karuna Therapeutics, Inc. from August of 2017 to December 2019. Dr. Chowrira received a J.D. from the University of Denver's Sturm College of Law, a Ph.D. in Molecular Biology from the University of Vermont College of Medicine, an M.S. in Molecular Biology from Illinois State University and a B.S. in Microbiology from the UAS, Bangalore, India.

Eric Elenko, Ph.D.
Chief Innovation and Strategy Officer

Eric Elenko, Ph.D., has served as our chief innovation officer since June 2015 and held various other positions at PureTech prior thereto. While at PureTech, Dr. Elenko has led the development of a number of programs, including Akili Interactive Labs, Gelesis, Karuna Therapeutics and Sonde Health. Dr. Elenko serves on the board of directors of Sonde. Prior to joining PureTech, Dr. Elenko was a consultant with McKinsey and Company from February 2002 to September 2005, where he advised senior executives of both Fortune 500 and specialty pharmaceutical companies on a range of issues such as product licensing, mergers and acquisitions, research and development strategy and marketing. Dr. Elenko received a B.A. in Biology from Swarthmore College and his Ph.D. in Biomedical Sciences from University of California, San Diego.

George Farmer, Ph.D.
Chief Financial Officer

George Farmer, Ph.D., has served as our chief financial officer since January 1, 2021. Dr. Farmer joined PureTech from BMO Capital Markets, where he completed a 15-year career as a senior biotechnology equity analyst providing in-depth sector research for institutional investor clients. Prior to this role, Dr. Farmer served as chief executive officer of Cortice Biosciences, a privately held biotechnology company focused on the clinical development of therapies for brain malignancies and neurodegenerative diseases. He also served as vice president of corporate development at Synta Pharmaceuticals, a publicly traded company developing cancer therapeutics. Dr. Farmer serves on the board of directors of Sonde Health, Inc. and Follica, Inc. Dr. Farmer was a postdoctoral fellow at Sloan Kettering Cancer Center and University of California San Francisco after receiving his Ph.D. in biological sciences from Columbia University and a BA from Dartmouth College.

Julie Krop, M.D.
Chief Medical Officer

Julie Krop, MD, is the chief medical officer at PureTech, where she is responsible for all clinical development, regulatory, CMC, and medical affairs for PureTech's clinical-stage Wholly Owned Pipeline. Prior to PureTech, Dr. Krop served as Chief Medical Officer at Freeline Therapeutics, a clinical-stage gene therapy company. She also previously served as Chief Medical Officer of AMAG Pharmaceuticals (acquired by Covis group for $647 million), where she oversaw clinical development, regulatory affairs, clinical operations, medical affairs, program management and pharmacovigilance. During her time at AMAG, Dr. Krop was responsible for the oversight of three FDA approvals. Earlier in her career, she held leadership positions at Vertex Pharmaceuticals, Stryker Regenerative Medicine, Peptimmune, Millennium Pharmaceuticals and Pfizer and also served on the board of directors of Aquestive Bio, Inc. Dr. Krop received her M.D. from Brown University School of Medicine and completed an internal medicine residency at Georgetown University Hospital. Additionally, she completed fellowships in epidemiology, clinical trial design and endocrinology as a Robert Wood Johnson Foundation Clinical Scholar at the Johns Hopkins School of Medicine.

Daphne Zohar
Founder and Chief Executive Officer, Member of the Board of Directors

Daphne Zohar is the founder of PureTech and has served as our chief executive officer and a member of our board of directors since our formation and UK main market listing in 2015 and served as the founding chief executive officer of a number of our Founded Entities. A successful entrepreneur, Ms. Zohar created PureTech, assembling a leading team and scientific network to help implement her vision for the company, and was a key participant in fundraising, business development and establishing the underlying programs and platforms that have resulted in PureTech's substantial pipeline which is comprised of 26 therapeutics and therapeutic candidates to date, including two therapeutics that have been cleared by the U.S. Food and Drug Administration for marketing and granted marketing authorization in the European Economic Area, or EEA. Ms. Zohar has been recognized as a top leader and innovator in biotechnology by a number of sources, including EY, BioWorld, MIT's Technology Review, the Boston Globe, and Scientific American. Ms. Zohar serves on the board of directors of Follica, Inc. Previously, Ms. Zohar has served on a number of private company boards including Karuna Therapeutics, Inc. and served on the board of resTORbio, Inc. (now Adicet Bio, Inc.) from December 2017-November 2018. Ms. Zohar received a B.S. from Northeastern University.

The Board

Roles and responsibilities of the Board

The Board is responsible to shareholders for our overall management as a whole. The main roles of the Board are:

- creating value for shareholders;
- providing business and scientific leadership;
- approving our strategic objectives;
- ensuring that the necessary financial and human resources are in place to meet strategic objectives;
- overseeing our system of risk management; and
- setting the values and standards for both our business conduct and governance matters.

The Directors are also responsible for ensuring that obligations to shareholders and other stakeholders are understood and met and that communication with shareholders is maintained. The responsibility of the Directors is collective, taking into account their respective roles as Executive Directors and Non-Executive Directors. All Directors are equally accountable to the Company's shareholders for the proper stewardship of its affairs and our long-term success.

The Board reviews strategic issues on a regular basis and exercises control over our performance by agreeing on budgetary and operational targets and monitoring performance against those targets. The Board has overall responsibility for our system of internal controls and risk management. Any decisions made by the Board on policies and strategy to be adopted by us or changes to current policies and strategy are made following presentations by the Executive Directors and other members of management, and only after a detailed process of review and challenge by the Board. Once made, the Executive Directors and other members of management are fully empowered to implement those decisions.

Except for a formal schedule of matters which are reserved for decision and approval by the Board, the Board has delegated our day-to-day management to the Chief Executive Officer who is supported by other members of the senior management team. The schedule of matters reserved for Board decision and approval are those significant to us as a whole due to their strategic, financial or reputational implications.

The Company's schedule of matters reserved for the Board includes the following matters:

- approval and monitoring of our strategic aims and objectives;
- approval of the annual operating and capital expenditure budget;
- changes to our capital structure, the issue of any of our securities and material borrowings;
- approval of the annual report and half-year results statement, accounting policies and practices or any matter having a material impact on our future financial performance;
- ensuring a sound system of internal control and risk management;
- approving Board appointments and removals, and approving policies relating to directors' remuneration;
- strategic acquisitions;
- major disposals of our assets or subsidiaries;
- approval of all circulars, prospectuses and other documents issued to shareholders governed by the Financial Conduct Authority's (FCA) Listing Rules, Disclosure Guidance and Transparency Rules or the City Code on Takeovers and Mergers;
- approval of terms of reference and membership of Board committees;
- considering and, where appropriate, approving directors' conflicts of interest; and
- approval, subject to shareholder approval, of the appointment and remuneration of the auditors.

The schedule of matters reserved to the Board is available on request from the Company Secretary or within the Investors section of our website at www.puretechhealth.com.

The Board delegates specific responsibilities to certain committees that assist the Board in carrying out its functions and ensure independent oversight of internal control and risk management. The three principal Board committees (Audit, Remuneration and Nomination) play an essential role in supporting the Board in fulfilling its responsibilities and ensuring that we maintain the highest standards of corporate governance. Each committee has its own terms of reference which set out the specific matters for which delegated authority has been given by the Board.

The terms of reference for each of the committees are fully compliant with the provisions of the Governance Code. All of these are available on request from the Company Secretary or within the Investors section of our website at www.puretechhealth.com.

Board size and composition

As of December 31, 2021, there were eight Directors on the Board: the Non-Executive Chair, two Executive Directors and five Non-Executive Directors. The biographies of these Directors are provided on pages 112 to 116. One of the Company's former Executive Directors, Mr. Stephen Muniz, retired from the Board and as Chief Operating Officer of the Company in May 2021. Dr. Bharatt Chowrira was appointed as an Executive Director in February 2021. There were no other changes to the composition of the Board during 2021. On March 24, 2022, Ms. Sharon Barber-Lui joined the Board as a non-Executive Director.

The Company's policy relating to the terms of appointment and the remuneration of both Executive and Non-Executive Directors is detailed in the Directors' Remuneration Report on pages 131 to 146.

The size and composition of the Board is regularly reviewed by the Nomination Committee to ensure there is an appropriate and diverse mix of skills and experience on the Board.

The Board may appoint any person to serve as a Director, either to fill a vacancy or as an addition to the existing Board. Any Director so appointed by the Board shall hold office only until the following AGM and then shall be eligible for election by the shareholders. In accordance with the Governance Code, all of the Directors will be offering themselves for election at the AGM to be held on June 15, 2022, full details of which are set out in the notice of meeting accompanying this Annual Report.

Non-Executive Directors

The Company's Non-Executive Directors are Mr. Christopher Viehbacher (Chair), Ms. Sharon Barber-Lui, Dr. Raju Kucherlapati, Dr. John LaMattina, Dr. Robert Langer, Ms. Kiran Mazumdar-Shaw and Dame Marjorie Scardino.

The Non-Executive Directors provide us with a wide range of skills and experience. Each Non-Executive Director has significant senior level experience as well as an extensive network in each of their own fields, an innovative mindset and independent judgement on issues of strategy, performance and risk, and is well placed to constructively challenge and scrutinize the performance of management. In addition, certain of our Non-Executive Directors also serve as members of one or more boards of directors of our Founded Entities and are key drivers for our Wholly Owned Pipeline.

Senior Independent Director

The Company's Senior Independent Director is Dame Marjorie Scardino. A key responsibility of the Senior Independent Director is to be available to shareholders in the event that they may feel it inappropriate to relay views through the Chair or Chief Executive Officer. In addition, the Senior Independent Director serves as an intermediary between the rest of the Board and the Chair where necessary. Further, the Senior Independent Director will lead the Board in its deliberations on any matters on which the Chair is conflicted.

The roles of Chair and Chief Executive Officer

The Company's Chair is Mr. Christopher Viehbacher. There is a clear division of responsibilities between the Chair and the Chief Executive Officer. Mr. Viehbacher was appointed Chair in September 2019.

The Chair is responsible for the leadership and conduct of the Board and for ensuring effective communication with shareholders.

The Chair facilitates the full and effective contribution of Non-Executive Directors at Board and Committee meetings, ensures that they are kept well informed and ensures a constructive relationship between the Executive Directors and Non-Executive Directors. The Chair also ensures that the Board committees carry out their duties, including reporting back to the Board either orally or in writing following their meetings at the next Board meeting.

The role of the Chief Executive Officer, Ms. Daphne Zohar, is to lead the execution of the Company's strategy and the executive management of PureTech. She is responsible, among other things, for the development and implementation of strategy and processes which enable us to meet the requirements of shareholders, for delivering the operating plans and budgets for our businesses, for monitoring business performance against key performance indicators (KPIs) and reporting on these to the Board and for providing the appropriate environment to recruit, engage, retain and develop the high-quality personnel needed to deliver our strategy.

Independence

The Governance Code requires that at least 50 percent of the Board of a UK premium listed company, excluding the Chair, consists of Non-Executive Directors determined by the Board to be independent in character and judgement and free from relationships or circumstances which may affect, or could appear to affect, the Directors' judgement. The Board regards Ms. Barber-Lui, Dr. Kucherlapati, Dr. LaMattina, Ms. Mazumdar-Shaw and Dame Marjorie Scardino as Independent Non-Executive Directors for the purposes of the Governance Code. In reaching this determination, the Board duly considered (i) their directorships and links with other Directors through their involvement in other subsidiary companies; (ii) their equity interests in PureTech and/or the Founded Entities, including equity grants of restricted stock units made to Non-Executive Directors by the Company under its Performance Share Plan; and (iii) in respect of Dr. LaMattina, the length of his tenure as a Director of the Company. The Board is satisfied that the judgement, experience and challenging approach adopted by each of these Directors should ensure that they each make a significant contribution to the work of the Board and its committees. Therefore, the Board has determined that Ms. Barber-Lui, Dr. Kucherlapati, Dr. LaMattina, Ms. Mazumdar-Shaw and Dame Marjorie Scardino are of independent character and judgement, notwithstanding the circumstances described at (i), (ii) and (iii) above.

Board support, indemnity and insurance

The Company Secretary, Dr. Bharatt Chowrira, is responsible to the Board for ensuring Board procedures are followed, applicable rules and regulations are complied with and that the Board is advised on governance and relevant regulatory matters. All Directors have access to the impartial advice and services of the Company Secretary.

There is also an agreed procedure for Directors to take independent professional advice at the Company's expense. In accordance with the Company's Articles of Association and a contractual Deed of Indemnity, the Directors have been granted an indemnity issued by the Company to the extent permitted by law in respect of liabilities incurred to third parties as a result of their office. The indemnity would not provide any coverage where a Director is proved to have acted fraudulently or with wilful misconduct. The Company has also arranged appropriate insurance cover in respect of legal action against its Directors and officers.

Board meetings and decisions

The Board meets regularly during the year, as well as on an ad hoc basis as required by business need. The Board had 4 scheduled meetings in 2021, and details on attendance are set forth in the table below:

Director	Number of Board Meetings Attended
Christopher Viehbacher	4/4
Raju Kucherlapati	4/4
John LaMattina	4/4
Robert Langer	4/4
Kiran Mazumdar-Shaw	4/4
Dame Marjorie Scardino	4/4
Bharatt Chowrira	4/4
Stephen Muniz	1/1
Daphne Zohar	4/4

While each director was able to attend every meeting in 2021, in the event of any unavoidable absence, the impacted Director would review with management the topics and materials to be discussed at the meeting, and provide appropriate feedback to be conveyed at such meeting.

The Board also acted by unanimous written consent five times in 2021. On occasion it was more expedient for the board to approve matters, especially administrative matters, by unanimous written consent rather than to convene a board meeting for the purpose. However, Directors were provided opportunity to discuss any concerns they had with the written resolution before its issue for signature.

At each meeting of the Board, there was a closed session held in which only the Chair and the other Non-Executive Directors participated.

The schedule of Board and Committee meetings each year is, so far as is possible, determined before the commencement of that year and all Directors or, if applicable, all Committee members, are expected to attend each meeting.

Supplementary meetings of the Board and/or the Committees are held as and when necessary. Each member of the Board receives in advance of each scheduled meeting detailed Board packages, which include an agenda based upon matters to be addressed and appropriate presentation and background materials. If a Director is unable to attend a meeting due to exceptional circumstances, he or she will nonetheless receive the meeting materials and discuss the materials with the Chief Executive Officer.

The Chair, Chief Executive Officer and senior management team work together to ensure that the Directors receive relevant information to enable them to discharge their duties and that such information is accurate, timely and clear. This information includes quarterly management accounts containing analysis of performance against budget as well as a summary of the operational performance of each of our businesses against its goals. Additional information is provided as appropriate for the topics being addressed at the meeting. At each meeting, the Board receives presentations from the Chief Executive Officer and, by invitation, other members of senior management as required. This ensures that all Directors are in a position to monitor effectively our overall performance, and to contribute to the development and implementation of its strategy.

The majority of Board meetings are held at our offices in Boston, Massachusetts, U.S., which gives members of the Company's senior management team, as well as the senior management of the Founded Entities, the opportunity to formally present to the Board on new technology development and business strategies. However, since the onset of the COVID-19 pandemic, for the safety of the Board and the Company's employees, all board meetings have been held by videoconference.

Certain Directors also serve on the boards of directors of our Founded Entities. These Founded Entity boards of directors meet regularly during the year, as well as on an ad hoc basis as required by business need. This service enables the Directors to have deep understanding of the businesses and contribute significantly to the strategy and oversight of these businesses.

Directors' conflicts of interest

Each Director has a statutory duty under the Companies Act 2006 (the CA 2006) to avoid a situation in which he or she has or can have a direct or indirect interest that conflicts or may potentially conflict with the interests of the Company. This duty is in addition to the continuing duty that a director owes to the Company to disclose to the Board any transaction or arrangement under consideration by the Company in which he or she is interested. The Company's Articles of Association permit the Board to authorize conflicts or potential conflicts of interest. The Board has established procedures for managing and, where appropriate, authorizing any such conflicts or potential conflicts of interest. In deciding whether to authorize any conflict, the Directors must have regard to their general duties under the CA 2006 and their overriding obligation to act in a way they consider, in good faith, will be most likely to promote the Company's success. In addition, the Directors are able to impose limits or conditions when giving authorization to a conflict or potential conflict of interest if they think this is appropriate. The authorization of any conflict matter, and the terms of any authorization, may be reviewed by the Board at any time. The Board believes that the procedures established to deal with conflicts of interest are operating effectively.

Induction, awareness and development

In preparation for the Company's initial public offering (IPO), all Directors received an induction briefing from the Company's legal advisors on their duties and responsibilities as Directors of a publicly quoted company. The Directors also received presentations from the Company's corporate brokers prior to the IPO. In addition, in order to ensure that the Directors continue to further their understanding of the challenges facing our Founded Entities and Wholly Owned Pipeline, the Board periodically receives the presentations and reports covering the business and operations of each of our Founded Entities as well as its Wholly Owned Pipeline.

We have put in place a comprehensive induction plan for any new Directors. This program will be tailored to the needs of each individual Director and agreed with him or her so that he or she can gain a better understanding of us and our businesses. In addition, the Company facilitates sessions as appropriate with our advisers, as well as appropriate governance specialists, to ensure that any new Directors are fully aware of, and understand, their responsibilities and obligations of a publicly quoted company and of the governance framework within which they must operate.

Board effectiveness and performance evaluation

The Board periodically reviews its effectiveness and performance. The Board seeks the assistance of an independent third-party provider at least once every three years in its evaluation in compliance with the Governance Code, and will otherwise carry out an internally facilitated Board evaluation led by the Senior Independent Director, assisted by the Company Secretary, covering the effectiveness of the Board as a whole, its individual Directors and its Committees.

In addition to the above, the Non-Executive Directors, led by the Senior Independent Director, will periodically appraise the Chair's performance, following which the Senior Independent Director will provide any feedback to the Chair. The performance of each of the Directors on the Board and the performance of the committees of the Board will be reviewed by the Chair as deemed necessary. The performance of Executive Directors will be reviewed by the Board on an ongoing basis, as deemed necessary, in the absence of the Executive Director under review.

Committees of the Board

The Board has three principal committees: the Nomination Committee, the Audit Committee and the Remuneration Committee. The composition of the three principal committees of the Board and the attendance of the members throughout the year is set out in the respective committee reports contained in this Annual Report. The terms of reference of each committee are available on request from the Company Secretary and within the Investors section of our website at www.puretechhealth.com.

Internal Control

The Board fully recognizes the importance of the guidance contained in the Guidance on Risk Management, Internal Control and Related Financial and Business Reporting. Our internal controls were in place during the whole of 2021, with a material weakness related to our risk assessment process over the design and implementation of our management review controls over the valuation of financial instruments, the completeness and accuracy of related sensitivity disclosures, the valuation of share based payment liabilities and completeness and the accuracy of the tax provision. We concluded that a similar material weakness existed in the prior financial period. During the year ended December 31, 2021, the Company took certain steps in its remediation plan, including (i) designing and documenting management review controls to address the level of aggregation and criteria for investigation, and (ii) implementing more robust procedures over the documentation of the performance of these management review controls. The Company has made progress toward remediation and will continue to implement its remediation plan for the ongoing material weaknesses in internal control over financial reporting described. The material weaknesses will not be considered remediated until the applicable controls operate for a sufficient period of time and management has concluded, through testing, that the controls are operating effectively. Additionally, in connection with the audit of our consolidated financial statements as of and for the year ended December 31, 2020, one of the identified material weaknesses related to a lack of segregation of duties with regard to uploading and posting journal entries in our previous ERP system. We deployed a new ERP system that went live on January 1, 2021, and as of December 31, 2021, this material weakness was remediated.

The Board is responsible for establishing and monitoring internal control systems and for reviewing the effectiveness of these systems. The Board views the effective operation of a rigorous system of internal control as critical to our success; however, it recognizes that such systems are designed to manage rather than eliminate risk of failure and can provide only reasonable and not absolute assurance against material misstatement or loss. The key elements of our internal control system, all of which have been in place during the financial year and up to the date these financial statements were approved, are as follows:

Control environment and procedures

We have a clear organizational structure with defined responsibilities and accountabilities. It adopts the highest values surrounding quality, integrity and ethics, and these values are communicated clearly throughout the whole organization. Detailed written policies and procedures have been established covering key operating and compliance risk areas. These policies and procedures are reviewed and the effectiveness of the systems of internal control is assessed periodically by the Board.

Identification and evaluation of risks

The Board actively identifies and evaluates the risks inherent in the business and ensures that appropriate controls and procedures are in place to manage these risks. The Board obtains an update regarding our Wholly Owned Pipeline and all Founded Entities on a regular basis and reviews our performance and the performance of our Wholly Owned Pipeline and Founded Entities on a quarterly basis. However, the performance of business units may be reviewed more frequently if deemed appropriate.

The key risks and uncertainties we face, as well as the relevant mitigations, are set out on pages 90 to 93 and in the Additional Information section from pages 217 to 251.

Information and financial reporting systems

We evaluate and manage significant risks associated with the process for preparing consolidated accounts by having in place systems and internal controls that ensure adequate accounting records are maintained and transactions are recorded accurately and fairly to permit the preparation of financial statements in accordance with IFRS. The Board approves the annual operating budgets and regularly receives details of actual performance measured against the budget.

Principal risks and uncertainties

Our operations and the implementation of our objectives and strategy are subject to a number of key risks and uncertainties. Risks are formally reviewed by the Board at least annually and appropriate procedures are put in place to monitor and, to the extent possible, mitigate these risks.

A summary of the key risks affecting us and the steps taken to manage these risks is set out on pages 90 to 93 and in the Additional Information section from pages 217 to 251.

Political expenditure

It is the Board's policy not to incur political expenditure or otherwise make cash contributions to political parties and it has no intention of changing that policy.

2022 Annual General Meeting

The Notice of the AGM, which will be held at 11:00 am EDT (4:00 pm BST) on June 15, 2022 at the Company's headquarters at 6 Tide Street in Boston, Massachusetts, U.S. is enclosed with this report. Details of the resolutions and the explanatory notes thereto are included with the Notice. To ensure compliance with the Governance Code, the Board proposes separate resolutions for each issue and proxy forms allow shareholders who are unable to attend the AGM to vote for or against or to withhold their vote on each resolution. In addition, to encourage shareholders to participate in the AGM process, the Company proposes to offer electronic proxy voting through the Registrar's website and through the CREST service. The results of all proxy voting will be published on our website after the AGM.

Our website at www.puretechhealth.com is the primary source of information on us. The website includes an overview of our activities, details of our businesses, and details of all of our recent announcements.

Relations with Stakeholders – Section 172 Statement

The Board recognizes its duties under Section 172 of the Companies Act 2006 and continuously has regard to how the Company's activities and decisions will impact investors, employees, those with whom it has a business relationship, the community and environment and its reputation for high standards of business conduct. In weighing all of the relevant factors, the Board, acting in good faith and fairly between members, makes decisions and takes actions that it considers will best lead to the long- term success of the Company. In accordance with Section 172, it is the responsibility of the Board as a whole to ensure that a satisfactory dialogue takes place and that the Board considers the potential impact on the Company's key stakeholders when making decisions.

The Board is committed to understanding and engaging with shareholders and other key stakeholder groups of the Company in order to maximize value and promote long-term Company success in line with our strategic objectives, as well as to promote and ensure fairness between our stakeholders. The Board believes that appropriate steps and considerations have been taken during the year so that each Director has an understanding of the various key stakeholders of the Company. The Board recognizes its responsibility to contemplate all such stakeholder needs and concerns as part of its discussions, decision-making, and in the course of taking actions and will continue to make stakeholder engagement a top priority in the coming years.

During the year, the Board assessed its current activities between the Board and its stakeholders, which demonstrated that the Board actively engages with its stakeholders and takes their various objectives into consideration when making decisions.

Stakeholder	How we engage	Key matters identified	Further information
Investors	• Our shareholders are the owners and investors in our business. We make significant efforts to engage with our shareholders and understand their objectives. We engage with our shareholders through a number of mechanisms to ensure that shareholder views are brought into the boardroom and considered in our decision-making. • The Board's primary shareholder contact is through the Chief Executive Officer. The Chair, the Senior Independent Director and other Directors, as appropriate, make themselves available for contact with major shareholders and other stakeholders in order to understand their issues and concerns. • Stakeholder engagement will often take place by the Executive Directors and senior management through investor meetings and investor roadshows, including participation at healthcare conferences and participating in fireside chats at those events, with the Board receiving regular updates by way of analysis reports on stakeholder views. • Meetings were held throughout the year with institutional shareholders. Key shareholder publications including the annual report, the full year and half year results announcements and press releases and the information for investors are available on the Company's website: www.puretechhealth.com.	• Our Board keeps its Strategy and Business Model under regular review. During the past year, the Board has engaged to carefully consider its strategy for future growth and development, in particular devoting attention to the future prospects of its business model and its listing venues and the risks and opportunities this would give to the Company's stakeholders. • The company carefully manages its expenditure and anticipates future capital needs through careful capital management and capital allocation to its Wholly Owned Programs and clinical trials as well as opportunities to secure financing from third parties, for example the $110m Series D financing for Akili in May 2021 and the $68m Series D financing for Vedanta in July 2021. Our Board also carefully considers opportunities for disposal of shares held in its Founded Entities such as the disposals of shares in Karuna raising $118m in February 2021 and $100m in November 2021. • During 2021, the Board welcomed Bharatt Chowrira to the Board as an Executive Director and saw the retirement of Steve Muniz as an Executive Director. The Board seeks to ensure appropriate board structure suitable for a Company of PureTech's size. • The Board recognizes the importance of Diversity, Equity and Inclusion and is delighted to be one of the few FTSE250 companies with a female CEO.	• Governance Section of ARA (Pages 90 to 146) • ESG Report (Pages 73 to 89) • Karuna disposals (Page 94) • Remuneration Report (Pages 131 to 146) • Value for Investors Section (Pages 23 to 34)

Stakeholder	How we engage	Key matters identified	Further information
Our People	• Our employees are crucial to the success of our business and many key decisions made by our Board have an impact on them. It is important to understand the employee perspective and ensure that we maintain an engaged workforce, as we believe that this will lead to better business results. We engage with our employees in various ways to ensure that their voice is heard in the management of our business including: – The conduct of regular Town Hall Meetings, email briefings to employees on key events as well as communication through the company intranet site and an engagement survey – The implementation of regular appraisals and personal development programs	• The Board recognizes the importance of an incentivized and engaged workforce, especially in the competitive greater Boston area. The Board engages to ensure the remuneration and benefit packages are competitive. • The Board aims to attract and retain employees through an established personal management and development program, with a view to development of the individual in an inclusive environment where employees from diverse backgrounds can thrive. • We are proud to be a company dedicated to discovering, developing and commercializing highly differentiated medicines for devastating diseases where limited or no treatment options currently exist for patients and believe we have established a business where our employees are proud to work.	• ESG Report (Pages 73 to 89) • Remuneration Report (Pages 131 to 146) • Strategic Report (Pages 1 to 72)
Community & Environment	• We are committed to supporting the communities in which we operate and the wider public. To that end, we have developed various mechanisms for engagement including: – Internships/partnerships with local universities and programs – Charitable giving – Building Certifications – Therapeutic Focus	• We are committed to improving our practices to ensure our business operates on a sustainable basis. In particular we have created an ESG committee chaired by one of our Non-Executive Directors to guide our sustainability initiatives. Our business Is a low carbon emissions and we are committed to delivering long term environmental sustainability. • We partner with local universities and programs to offer paid internship and externship programs, generally within technical fields in our development organization. • The company engages with local community and supports charitable causes. In particular, in 2021 and through the January 2022 post-period, PureTech made charitable contributions to Life Sciences Cares, The Greater Boston Food Bank (GBFB), Lymphatic Education & Research Network (LE&RN), Langer Prize for Innovation & Entrepreneurial Excellence Fellowship, and Fred Hutchinson Cancer Research Center.	• ESG Report (Pages 73 to 89) • LYT-100 Long COVID Study (Page 26)
Suppliers/ Business Partners	• Our business model creates value through partnerships and relationships with various key collaborators, and we continually evaluate how to strengthen relationships and arrangements with these institutions and individuals. Our engagement in 2021 included: – Quality updates and quality audits – Meetings with key surgeons to understand/identify potential indications and applications for therapeutics – Partnerships – Imbrium, BeiGene, Eli Lilly	• We aim to build clear and reliable supply arrangements with our contract manufacturers for clinical product supply, in particular with an emphasis on quality, especially in relation to a clinical environment. • We seek partnerships with other life sciences organizations to secure non-dilutive funding, access to development opportunities, and access to materials for our clinical trials.	• Value for Investors (Pages 23 to 34) • LYT-503/IMB-150 (Page 50) • LYT-200 (Pages 41 to 43) • Entrega (Page 72)

Directors' Report for the year ended December 31, 2021

The Directors present their report and the audited consolidated financial statements for the financial year ended December 31, 2021.

Certain disclosure requirements for inclusion in this report have been incorporated by way of cross reference to the Strategic Report, the Directors' Remuneration Report and the ESG Report which should be read in conjunction with this report.

The Company was incorporated on May 8, 2015 as a public company limited by shares in the UK and has a registered office situated at 8th Floor, 20 Farringdon Street, London, EC4A 4AB, United Kingdom. The Company was admitted to the premium listing segment of the Official List of the UK Listing Authority and to trading on the main market of the London Stock Exchange on June 24, 2015. The Company's American Depository Shares, each representing 10 ordinary shares, began trading on the Nasdaq Global Market on November 16, 2020.

Directors

The membership of the Board can be found below, and biographical details of the directors can be found on pages 112 to 116 and are deemed to be incorporated into this report.

Descriptions of the terms of the directors' service contracts are set forth on page 137 and page 144 of this report.

All directors shall retire from office and will offer themselves for reappointment by the members at the Company's upcoming AGM.

Details of the interests of directors in the share capital of the Company as of December 31, 2021 are set out in the Annual Report on Remuneration on page 144 and Note 24 to the financial statements, located on page 207. There have been no changes in such interests from December 31, 2021 to March 31, 2022, except as specifically set forth in those sections.

Results and dividends

We generated a loss for the year ended December 31, 2021 of $62.7 million (2020: income of $4.5 million).

The Directors do not recommend the payment of a dividend for the year ended December 31, 2021 (2020: nil).

Share capital

As of December 31, 2021, the ordinary issued share capital of the Company stood at 287,796,585 shares of £0.01 each, including shares issuable upon conversion of outstanding ADSs. Details on share capital are set out in Note 14 to the financial statements, page 191.

The Company's issued ordinary share capital comprises a single class of ordinary shares. Details on movements in issued share capital can be found in Note 14 to the financial statements, page 191.

Rights of ordinary shares

All of the Company's issued ordinary shares are fully paid up and rank pari passu in all respects and there are no special rights with regard to control of the Company. There are no restrictions on the transfer of ordinary shares or on the exercise of voting rights attached to them, which are governed by the Articles of Association and relevant UK legislation. The Directors are not aware of any agreements between holders of the Company's shares that may result in restrictions on the transfer of securities or in voting rights.

The shares in the Company issued to former holders of Ariya Therapeutics Inc. securities were subject to lock up agreements with the Company and were not tradable until such restrictions lapsed on October 1, 2021.

Substantial shareholders

As of March 31, 2022, the Company had been advised that the shareholders listed on page 124 hold interests of 3 percent or more in its ordinary share capital (other than interests of the Directors which are detailed on page 144 of the Directors' Remuneration Report). Other than as shown, so far as the Company (and its Directors) are aware, no other person holds or is beneficially interested in a disclosable interest in the Company.

Powers of the Directors

Subject to the Company's Articles of Association, UK legislation and any directions given by special resolution, the business of the Company is managed by the Board of Directors. Details of the matters reserved for the Board can be found in the Corporate Governance Report on page 117.

Articles of Association

The Articles of Association of the Company can only be amended by special resolution at a general meeting of the shareholders. No amendments are proposed at The 2022 AGM.

Ms. Sharon Barber-Lui was appointed to the Board as a Non-Executive Director on March 24, 2022.
The following have served as Directors of the Company during the 2021 financial year.

Name	Role	Age (as of December 31, 2021)
Mr. Christopher Viehbacher	Non-Executive Chair	61
Ms. Daphne Zohar	Chief Executive Officer	51
Dame Marjorie Scardino	Senior Independent Director	74
Dr. Robert Langer	Non-Executive Director	73
Dr. Raju Kucherlapati	Independent Non-Executive Director	78
Dr. John LaMattina	Independent Non-Executive Director	71
Ms. Kiran Mazumdar-Shaw	Independent Non-Executive Director	68
Dr. Bharatt Chowrira	President; Chief Business, Legal and Operating Officer; Company Secretary (appointed February 2021)	56
Mr. Stephen Muniz	Chief Operating Officer (retired May 2021)	51

Directors' liabilities (Directors' indemnities)

As at the date of this report, the Company has granted qualifying third party indemnities to each of its Directors against any liability that attaches to them in defending proceedings brought against them, to the extent permitted by the Companies Act. In addition, Directors and officers of the Company and its Founded Entities have been and continue to be covered by directors' and officers' liability insurance.

See further description of indemnity and insurance on page 118.

Political donations

No political contributions/donations for political purposes were made by the Company or any of our affiliate companies to any political party, politician, elected official or candidate for public office during the financial year ended December 31, 2021 (2020: nil).

Significant agreements

There are no agreements between the Company or any of our affiliate companies and any of its employees or any Director which provide for compensation to be paid to an employee or a Director for loss of office as a consequence of a takeover of the Company.

Compliance with the UK Corporate Governance Code

The Directors are committed to a high standard of corporate governance and compliance with the best practice of the UK Corporate Governance Code (Governance Code) published in July 2018. The Governance Code is available at the Financial Reporting Council website at www.frc.org.uk.

The Directors consider that the Company has, throughout the year ended December 31, 2021, applied the main principles and complied with the provisions set out in the Governance Code with the following exception: contrary to provision 24 of the Governance Code, the Chair, Mr. Christopher Viehbacher, was also Chair of the Audit Committee in 2021. The Board believes that Mr. Viehbacher's professional background and experience, together with his past participation on such committee for the past five years, made him a valuable member of the Audit Committee and that his membership was in the best interests of the Company's shareholders. Mr. Viehbacher was appointed Chair in September 2019. Immediately following the publication of its Annual Report and Accounts for the year ended December 31, 2021, Ms. Sharon Barber-Lui will become the Chair of the Audit Committee, and Mr. Viehbacher will step down as the Chair of the Audit Committee but remain a member thereof.

Further explanation as to how the provisions set out in the Governance Code have been applied by the Company is provided in this Report, the Report of the Nomination Committee and the Report of the Audit Committee.

Financial instruments

The financial risk management and internal control processes and policies, and exposure to the risks associated with financial instruments can be found in Note 16 to the financial statements and the Corporate Governance section of the Annual Report on page 129.

Sustainable development and environmental matters

Details of the Company's policies and performance, as well as disclosures concerning GHG emissions, are provided in the ESG Report on pages 73 to 89.

Related party transactions

Details of related party transactions can be found in Note 24 of the financial statements on pages 206 to 207.

Issuances of equity by major subsidiary undertaking

In April 2021 and November 2021, Sonde issued convertible promissory notes in the principal aggregate amount of $4.3 million. PureTech Health LLC participated and invested $2.1 million in the notes.

In July 2021, Vedanta completed Its Series D financing round In which It Issued and sold an aggregate of 2,387,675 shares of preferred stock for aggregate proceeds of approximately $68 million, of which purchased 174,520 shares for an aggregate purchase price of $5.0 million.

Future business developments

Information on the Company and its Wholly Owned Pipeline and Founded Entities' future developments can be found in the Strategic Report on pages 35 to 72.

Risk and internal controls

The principal risks we face are set out on pages 90 to 93 and in the Additional Information section from pages 217 to 251. The Audit Committee's assessment of internal controls is laid out on page 129.

Subsequent Events

Research and Development

Information on our research and development activities can be found in the Strategic Report on pages 35 to 72.

Going concern

As of December 31, 2021, the directors had a reasonable expectation that we had adequate resources to continue in operational existence into the first quarter of 2025.

Shareholder	%
Invesco Asset Management Limited	22.51
Baillie Gifford & Co	10.28
Lansdowne Partners International Limited	8.66
M&G Investment Management, LTD	4.20
Miller Value Partners	3.66
Recordati SA	3.32

* Represents an entity that is not a major subsidiary undertaking of the Company.

Annual General Meeting

The Notice of the AGM, which will be held at 11:00 am EDT (4:00 pm BST) on June 15, 2022 at the Company's headquarters at 6 Tide Street in Boston, Massachusetts, U.S. is enclosed with this report. Details of the resolutions and the explanatory notes thereto are included with the Notice. To ensure compliance with the Governance Code, the Board proposes separate resolutions for each issue and proxy forms allow shareholders who are unable to attend the AGM to vote for or against or to withhold their vote on each resolution. In addition, to encourage shareholders to participate in the AGM process, the Company proposes to offer electronic proxy voting through the Registrar's website and through the CREST service. The results of all proxy voting will be published on our website after the AGM.

The Notice of the Meeting, together with an explanation of the items of business, will be contained in a circular to shareholders to be dated April 26, 2022.

Pension schemes

Information on the Company's 401K Plan can be found in the Annual Report on Remuneration on page 133.

Disclosure of information under Listing Rule 9.8.4R

For the purposes of LR 9.8.4R, the information required to be disclosed can be found in the sections of the Annual Report and Financial Statements listed in the table below.

Listing Rule Requirement	Location in Annual Report
A statement of the amount of interest capitalized during the period under review and details of any related tax relief.	N/A
Information required in relation to the publication of unaudited financial information.	N/A
Details of any long-term incentive schemes.	Directors' Remuneration Report, page 131
Details of any arrangements under which a Director has waived emoluments, or agreed to waive any future emoluments, from the Company.	N/A
Details of any non-pre-emptive issues of equity for cash.	N/A
Details of any non-pre-emptive issues of equity for cash by any unlisted major subsidiary undertaking.	Directors' Report, page 124
Details of parent participation in a placing by a listed subsidiary.	N/A
Details of any contract of significance in which a Director is or was materially interested.	N/A
Details of any contract of significance between the Company (or one of its subsidiaries) and a controlling shareholder.	N/A
Details of any provision of services by a controlling shareholder.	N/A
Details of waiver of dividends or future dividends by a shareholder.	N/A
Where a shareholder has agreed to waive dividends, details of such waiver, together with those relating to dividends which are payable during the period under review.	N/A
Board statements in respect of relationship agreement with the controlling shareholder.	N/A

Whistleblowing, anti-bribery and corruption

We seek at all times to conduct our business with the highest standards of integrity and honesty. We also have an anti-bribery and corruption policy which prohibits our employees from engaging in bribery or any other form of corruption. In addition, we have a whistleblowing policy under which staff are encouraged to report to the Chief Executive Officer or the President, any alleged wrongdoing, breach of a legal obligation or improper conduct by or on the part of us or any of our officers, Directors, employees, consultants or advisors.

Appointment of auditor

KPMG LLP, the external Auditor of the Company, was appointed in 2015 and a resolution proposing its reappointment will be proposed at the forthcoming AGM.

Disclosure of information to auditor

The Directors who held office at the date of approval of this Directors' report confirm that:

- so far as the Director is aware, there is no relevant audit information of which the Company's Auditor is unaware; and
- the Director has taken all steps that he/she ought to have taken as a Director in order to make himself/herself aware of any relevant audit information and to establish that the Company's Auditor is aware of that information.

This confirmation is given and should be interpreted in accordance with the provisions of Section 418 of the CA 2006.

Statement of Directors' responsibilities in respect of the Annual Report and the financial statements

The directors are responsible for preparing the Annual Report and the Group and parent Company financial statements in accordance with applicable law and regulations.

Company law requires the directors to prepare Group and parent Company financial statements for each financial year. Under that law they are required to prepare the Group financial statements in accordance with UK-adopted international accounting standards and applicable law and have elected to prepare the parent Company financial statements on the same basis. In addition, the Group financial statements are required under the UK Disclosure Guidance and Transparency Rules to be prepared in accordance with the UK-adopted international accounting standards.

Under company law the directors must not approve the financial statements unless they are satisfied that they give a true and fair view of the state of affairs of the Group and parent Company and of the Group's profit or loss for that period. In preparing each of the Group and parent Company financial statements, the directors are required to:

- select suitable accounting policies and then apply them consistently;
- make judgements and estimates that are reasonable, relevant and reliable;
- state whether they have been prepared in accordance with the UK-adopted international accounting standards;
- assess the Group and parent Company's ability to continue as a going concern, disclosing, as applicable, matters related to going concern; and
- use the going concern basis of accounting unless they either intend to liquidate the Group or the parent Company or to cease operations, or have no realistic alternative but to do so.

The directors are responsible for keeping adequate accounting records that are sufficient to show and explain the parent Company's transactions and disclose with reasonable accuracy at any time the financial position of the parent Company and enable them to ensure that its financial statements comply with the Companies Act 2006. They are responsible for such internal control as they determine is necessary to enable the preparation of financial statements that are free from material misstatement, whether due to fraud or error, and have general responsibility for taking such steps as are reasonably open to them to safeguard the assets of the Group and to prevent and detect fraud and other irregularities.

Under applicable law and regulations, the directors are also responsible for preparing a Strategic Report, Directors' Report, Directors' Remuneration Report and Corporate Governance Statement that complies with that law and those regulations.

The directors are responsible for the maintenance and integrity of the corporate and financial information included on the company's website. Legislation in the UK governing the preparation and dissemination of financial statements may differ from legislation in other jurisdictions.

Responsibility statement of the directors in respect of the annual financial report

We confirm that to the best of our knowledge:

- the financial statements, prepared in accordance with the applicable set of accounting standards, give a true and fair view of the assets, liabilities, financial position and profit or loss of the company and the undertakings included in the consolidation taken as a whole; and
- the strategic report includes a fair review of the development and performance of the business and the position of the issuer and the undertakings included in the consolidation taken as a whole, together with a description of the principal risks and uncertainties that they face.

We consider the annual report and accounts, taken as a whole, is fair, balanced and understandable and provides the information necessary for shareholders to assess the Group's position and performance, business model and strategy.

By Order of the Board

Daphne Zohar
Founder, Chief Executive Officer and Director

April 25, 2022

Report of the Nomination Committee

Dame Marjorie Scardino
Chair, Nomination Committee

Committee responsibilities

The Nomination Committee assists the Board in discharging its responsibilities relating to the composition and make-up of the Board and any Committees of the Board. It is also responsible for periodically reviewing the Board's structure and identifying potential candidates to be appointed as Directors or Committee members as the need may arise. The Nomination Committee is responsible for evaluating the balance of skills, knowledge and experience and the size, structure and composition of the Board and Committees of the Board, retirements and appointments of additional and replacement Directors and Committee members, and makes appropriate recommendations to the Board on such matters. A full copy of the Committee's Terms of Reference is available on request from the Company Secretary and within the Investor's section on Company's website at www.puretechhealth.com.

Committee membership

The Nomination Committee consisted of Dame Marjorie Scardino, who served as the committee's Chair, Dr. Robert Langer, and Ms. Kiran Mazumdar-Shaw. The biographies of the Nomination Committee members can be found on pages 112 to 113.

The Governance Code requires that a majority of the members of a nomination committee should be independent Non-Executive Directors.

In making their determination for the year 2021, the Board regarded Dame Marjorie Scardino, Dr. Langer and Ms. Mazumdar-Shaw as meeting the independence criteria set out in the Governance Code as it is applied to their service on the Nomination Committee. In reaching this determination, the Board duly considered (i) their directorships and links with other Directors through their involvement in other Founded Entities; (ii) their equity interests in PureTech Health and/or the Founded Entities; and (iii) the circumstance that Dr. Langer is a founding Director of the Company. The Board also duly considered the extent to which these matters may impact their service on the Nomination Committee. After such consideration, the Board has determined Dame Marjorie Scardino, Dr. Langer and Ms. Mazumdar-Shaw to be independent in character and judgement and free from relationships or circumstances which might affect, or appear to affect, the Directors' judgement in their service on the Nomination Committee.

The Nomination Committee meets as required to initiate the selection process of, and make recommendations to, the Board with regard to the appointment of new Directors. During 2021, the Nomination Committee met one time to review the structure, size and composition of the Board in light of the requirements of the Governance Code. Dame Marjorie Scardino and Dr. Langer participated in the meeting. The Chief Executive Officer and the President were invited to and attended the meeting.

Diversity policy

Diversity within the Company's Board is essential in maximizing its effectiveness, as it enriches debates, business planning and problem-solving. The Company approaches diversity in its widest sense so as to recruit the best talent available, based on merit and assessed against objective criteria of skills, knowledge, independence and experience as well as other criteria such as gender, age and ethnicity. The Company will adhere to a strategy of recruiting individuals who meet these criteria as it searches for additional independent Non-Executive Directors to the Board, as discussed below. The Committee's primary objective is to ensure that the Company maintains the strongest possible leadership.

Information regarding the Company's diversity efforts can be found in the ESG Report on pages 73 to 89.

Board and Committee evaluation

Information regarding the evaluation of the Board and its Committees can be found on page 119.

Report of the Audit Committee

Mr. Christopher Viehbacher
Chair, Audit Committee

Committee responsibilities

The Audit Committee monitors the integrity of our financial statements and reviews all proposed annual and half-yearly results announcements to be made by us with consideration being given to any significant financial reporting judgements contained in them. The Committee also advises the Board on whether it believes the annual report and accounts, taken as a whole, are fair, balanced and understandable and provide the information necessary for shareholders to assess the Company's position and performance, business model and strategy. The Committee also considers internal controls, compliance with legal requirements, the FCA's Listing Rules, Disclosure Guidance and Transparency Rules, and reviews any recommendations from the Group's Auditor regarding improvements to internal controls and the adequacy of resources within our finance function. A full copy of the Committee's Terms of Reference is available on request from the Company Secretary and within the Investor's section on the Company's website at www.puretechhealth.com.

Committee membership

The Committee consisted of three independent Non-Executive Directors, Mr. Christopher Viehbacher, Dr. Raju Kucherlapati and Dame Marjorie Scardino, until Ms. Sharon Barber-Lui joined the Committee upon her appointment to the Board on March 24, 2022. Mr. Viehbacher served as Chair of the Committee. Mr. Viehbacher has experience as a Chartered Accountant and has held numerous senior executive positions in his career. The Board has deemed this to be recent and relevant financial experience, qualifying him to be Chair of the Committee. The biographies of the Committee members can be found on pages 112 to 113. The Committee met four times during the year, with Mr. Viehbacher, Dr. Kucherlapati and Dame Marjorie Scardino each attending all four meetings. The Chief Financial Officer and the external Auditor were invited to and attended all of the meetings. The Chief Executive Officer and President also attended certain of the meetings. When appropriate, the Committee met with the Auditor without any members of the executive management team being present. Immediately following the Company's publication of Its Annual Report and Accounts for the year ended December 31, 2021, Ms. Barber-Lui will become the Chair of the Audit Committee, and Mr. Viehbacher will step down as the Chair of the Audit Committee but remain a member thereof. Ms. Barber-Lui has accounting experience, is currently the Senior Vice President of Finance at EQRx, Inc., a publicly-traded U.S. company (Nasdaq: EQRX), and has held a number of senior finance and executive leadership positions In her career. The Board has deemed this to be recent and relevant financial experience qualifying her to be Chair of the Committee.

Activities during the year

The activities undertaken by the Committee were the normal recurring items, the most important of which are noted below.

Significant issues considered in relation to the financial statements

The Committee considered, in conjunction with management and the external auditor, the significant areas of estimation, judgement and possible error in preparing the financial statements and disclosures, discussed how these were addressed and approved the conclusions of this work. The principal areas of focus in this regard were:

Valuation of investments and intercompany receivable balances held by the Parent Company

The significant issue is the recoverability of the investment by the Company, due to its materiality in the context of the total assets of the Company. The carrying value of investments in Founded Entities and intercompany receivables is supported by our underlying assets. The Committee was satisfied with the conclusion reached.

Valuation of financial instruments; investments in Gelesis and Akili preferred share financial assets, Vedanta and Follica preferred shares financial liabilities and Follica and Vedanta warrants financial liabilities

An area of material judgement in our financial statements and, therefore, audit risk relates to the valuation of third party held preferred shares classified as liabilities, convertible loan notes and warrants measured at fair value through profit/loss, which at year end had a carrying value totaling $183 million (2020 – $152 million), as well as investments held at fair value that do not have a quoted active market price which at year end had a carrying value totaling $240 million (2020 – $207 million). We considered the underlying economics of the valuations of the Founded Entities and the investees and sought external expertise in determining the appropriate valuation of the liabilities and investments. These valuations rely, in large part, on the valuation of our programs and values of recent transactions and determine the amount of gain (loss) on the financial instruments.

Classification of new preferred shares and convertible loan notes including identification and classification of any embedded derivatives

As part of our strategy to finance the Founded Entities, we issue financial instruments commensurate with the economics of each transaction. These financial instruments can include preferred shares, convertible notes, warrants and loans payable. Often these arrangements contain terms that can make it difficult to determine whether the financial instrument should be classified as debt or equity on our statement of financial position. We considered the pertinent terms and underlying economics of the financial instruments and have appropriately classified them as debt or equity. The Committee believes that we considered the pertinent terms and underlying economics of each of the financial instruments, as well as the advice of external experts, and has appropriately classified them as debt or equity.

Regulatory compliance

Ensuring compliance for FCA regulated businesses also represents an important control risk from the perspective of the Committee. We engage with outside counsel and other advisors on a regular basis to ensure compliance with legal requirements.

Review of Annual Report and Accounts and Half-yearly Report

The Committee carried out a thorough review of our 2021 Annual Report and Accounts and our 2021 Half-yearly Report resulting in the recommendation of both for approval by the Board. In carrying out its review, the Committee gave particular consideration to whether the Annual Report, taken as a whole, was fair, balanced and understandable, concluding that it was. It did this primarily through consideration of the reporting of our business model and strategy, the competitive landscape in which it operates, the significant risks it faces, the progress made against its strategic objectives and the progress made by, and changes in fair value of, its Founded Entities during the year.

Going concern

At least annually, the Committee considers the going concern principle on which the financial statements are prepared. As a business which seeks to fund the development of its Wholly Owned Pipeline, as well as support its Founded Entities with further capital, the business model is currently inherently cash consuming.

As of December 31, 2021, we had sufficient cash reserves to extend operations over a three-year period into the first quarter of 2025.

Therefore, while an inability of the Wholly Owned Pipeline and Founded Entities to raise funds through equity financings with outside investors, strategic arrangements, licensing deals or debt facilities may require us to modify our level of capital deployment into our Wholly Owned Pipeline and Founded Entities or to more actively seek to monetize one or more Founded Entities, it would not threaten our viability overall.

Compliance

The Committee has had a role in supporting our compliance with the Governance Code, which applies to us for the 2021 financial year. The Board has included a statement regarding our longer-term viability on page 94. The Committee worked with management and assessed that there is a robust process in place to support the statement made by the Board.

Similarly, the Committee worked with management to ensure that the current processes underpinning its oversight of internal controls provide appropriate support for the Board's statement on the effectiveness of risk management and internal controls.

Risk and internal controls

The principal risks we face are set out on pages 70 to 73 and in the Additional Information section from pages 217 to 251.

The Committee has directed that management engage in a continuous process to review internal controls around financial reporting and safeguarding of assets. Management has engaged external advisors to complete internal control testing on behalf of management for the 2021 financial year and the results were presented to the Committee. With the exception of the material weakness related to our risk assessment process over the design and implementation of our management review controls over the valuation of financial instruments, the completeness and accuracy of related sensitivity disclosures, the valuation of share based payment liabilities and completeness and the accuracy of the tax provision, the Committee believes that we have adequate controls and appropriate plans to evolve the control structure in anticipation of increased complexity of the business model and operations.

We have a formal whistleblowing policy. The Committee is satisfied that the policy has been designed to encourage staff to report suspected wrongdoing as soon as possible, to provide staff with guidance on how to raise those concerns, and to ensure staff that they should be able to raise genuine concerns without fear of reprisals, even if they turn out to be mistaken.

Internal audit

We do not maintain a separate internal audit function. This is principally due to our size, where close control over operations is exercised by a small number of executives. In assessing the need for an internal audit function, the Committee considered the risk assessment performed by management to identify key areas of assurance and the whole system of internal financial and operational controls. The Company achieves internal assurance by performing the risk assessment of the key areas of assurance and maintaining related key internal controls.

External audit

We have engaged KPMG LLP as our Auditor since 2015. The current audit partner is Robert Seale who has been our audit partner since June 2019.

The effectiveness of the external audit process is dependent on appropriate risk identification. In October 2021, the Committee discussed the Auditor's audit plan for 2021. This included a summary of the proposed audit scope and a summary of what the Auditor considered to be the most significant financial reporting risks facing us together with the Auditor's proposed audit approach to these significant risk areas. The main areas of audit focus for the year were (a) the valuation of investments and intercompany receivable balances held by the Parent Company, (b) Valuation of financial instruments; investments in Gelesis and Akili preferred share financial assets, Vedanta and Follica preferred shares financial liabilities and Follica and Vedanta warrants financial liabilities and (c) Classification of new preferred shares and convertible loan notes including identification and classification of any embedded derivatives.

Appointment and independence

The Committee advises the Board on the appointment of the external Auditor and on its remuneration both for audit and non-audit work, and discusses the nature, scope and results of the audit with the external Auditor. The Committee keeps under review the cost-effectiveness and the independence and objectivity of the external Auditor. Controls in place to ensure this include monitoring the independence and effectiveness of the audit, a policy on the engagement of the external Auditor to supply non-audit services, and a review of the scope of the audit and fee and performance of the external Auditor.

The Audit Committee ensures that at least once every ten years the audit services contract is put out to tender to enable us to compare the quality and effectiveness of the services provided by the incumbent auditor with those of other audit firms.

Non-audit work

The Committee approves all fees paid to the Auditor for non-audit work.

Where appropriate, the Committee sanctions the use of KPMG LLP for non-audit services in accordance with our non-audit services policy. During 2021 KPMG LLP did not provide any non-audit related services. Therefore the ratio of non-audit work to audit work was nil, which the committee is satisfied does not breach the independence of KPMG LLP.

Christopher Viehbacher
Chair of Audit Committee

April 25, 2022

Directors' Remuneration Report for the year ended December 31, 2021

Dr. John LaMattina
Chair,
Remuneration
Committee

The Directors' Remuneration Report is split into three sections, namely:

- This Annual Statement: summarizing and explaining the major decisions on Directors' remuneration in the year;
- The Directors' Remuneration Policy: setting out the framework for remuneration for our Directors in 2022 on pages 133 to 137; and
- The Annual Report on Remuneration: setting out the implementation of the Remuneration Policy in the year ended December 31, 2021 on pages 138 to 146.

The Company puts the Directors' Remuneration Policy to a binding vote of our shareholders every three years (sooner if changes are required to the Policy). The Annual Report on Remuneration is subject to an annual advisory vote of our shareholders.

The current Directors' Remuneration Policy was last approved at the 2021 AGM, and such approval is effective until the 2024 AGM. The Annual Report on Remuneration will be subject to an advisory shareholder vote at the forthcoming 2022 AGM.

Committee responsibilities

The Remuneration Committee's primary purpose is to assist the Board in determining the Company's remuneration policies. The Remuneration Committee has the responsibility for setting the remuneration policy for all Executive Directors and the Chairman of the Company, including pension rights and compensation payments, and in determining such policy must take into account all factors which it deems necessary including regulatory requirements, with the objective of attracting, retaining and motivating executive management having regard to views of shareholders and stakeholders and the risk appetite of the Company and alignment to the Company's long term goals and strategic plan. The Remuneration Committee also recommends and monitors the level and structure of remuneration for senior management.

The Remuneration Committee shall, in consultation with the Chairman and/or the Chief Executive Officer, determine the total individual remuneration package of each Executive Director, including share awards. The Remuneration Committee shall also have regard to current information for remuneration in other companies of comparable scale and complexity and can appoint remuneration consultants to assist in such process. The Remuneration Committee also has responsibility to review the design of all share incentive plans and determine awards under such plans. A full copy of the Remuneration Committee's Terms of Reference is available on request from the Company Secretary and within the Investors section of the Company's website at www.puretechhealth.com.

Committee membership

The Remuneration Committee consists of Dr. Kucherlapati, Dr. LaMattina and Ms. Mazumdar-Shaw, with Dr. LaMattina serving as Chair of the Committee. The biographies of the Committee members can be found on pages 112 to 113. The Committee met three times during the year, with each Committee member in attendance for all of the meetings. The Committee also acted by unanimous written consent five times during the year. The Chief Executive Officer and the Chief Operating Officer were invited to and attended all of the meetings, with Mr. Muniz attending each of the two meetings prior to his retirement in May 2021. Dr. Chowrira was invited to and attended the Committee meeting occurring after Mr. Muniz's retirement. However, no Executive Director was permitted to participate in discussions or decisions about his or her personal remuneration.

Our Remuneration Policy

The success of PureTech depends on the motivation and retention of our highly skilled workforce with significant expertise across a range of science and technology disciplines, as well as our highly-experienced management team and seasoned Directors. PureTech's Remuneration Policy is therefore an important part of our business strategy. Our guiding principle is to provide market competitive remuneration packages, including with respect to cash compensation in the form of base salary, annual bonuses and benefits as well as share based compensation, benchmarked against data generated from our local markets to enable us to put together and retain a top tier team.

The Directors' Remuneration Policy was approved by shareholders at the 2021 AGM with 89.3% support. Whilst the Committee was pleased with the support received, as part of the engagement process with shareholders for determining the policy, the Committee understood that some shareholders had concerns with the increase to quantum of the share based awards. Share based remuneration is a vital component of the remuneration packages of both executives and the Board of Directors and allows us to compete for, attract and retain talent in the U.S. market.

We remain committed to long-term performance-based remuneration delivered through our Performance Share Plan ("PSP") and believe that our current remuneration policy provides an appropriate framework to incentivize and motivate our senior management team with competitive U.S. remuneration packages, while also ensuring the structure of the PSP is aligned to UK practice.

All tables within the Directors' Remuneration Report are audited under the International Standards on Auditing (UK) ("ISAs (UK)") unless otherwise noted.

Objectives of the Remuneration Policy for our CEO and Senior Executives

In the construction of our senior executive Remuneration Policy, the Committee paid particular regard to the market practice of U.S. peer companies to ensure that packages are competitive, recognizing the predominantly U.S. market in which we compete for talent. At the same time, the structure of the packages was designed to be in line with the principles of the UK Corporate Governance Code and best practice.

The key aims of the Remuneration Policy and the Code principles to which they relate are as follows:

- promote our long-term success (Code principle: Proportionality);
- attract, retain and motivate high caliber senior management and focus them on the delivery of our long-term strategic and business objectives (Proportionality, alignment to culture and risk);
- be simple and understandable, both externally and internally (Clarity, simplicity, predictability and proportionality);

- achieve consistency of approach across senior management to the extent appropriate and informed by relevant market benchmarks (Clarity and alignment to culture); and
- encourage widespread equity ownership across the executive team to ensure a long-term focus and alignment of interest with shareholders (Alignment to culture, risk).

Performance and reward in 2021, and our response to the COVID-19 pandemic

One of our key business priorities during 2021 continued to be the health and well-being of our employees in light of the ongoing COVID-19 pandemic. We were pleased with the performance of our workforce under conditions that continued to require the development of new ways of working, in many cases from home, and we have supported our employees with several initiatives based around their welfare. These initiatives included extensive health protocols for those required to be onsite, flexible work from home arrangements, required vaccinations and a 100% company vaccination rate, assistance with safe transportation and a program to bring lunch into the office for those onsite, among others. As in 2020, we did not need to receive any Government support in 2021 and furthermore our operational and financial performance has not been significantly impacted by the pandemic.

During 2021, PureTech delivered exceptional execution and achievement of key strategic and financial goals, which has been reflected in the annual bonus and PSP outcomes. The Company delivered substantial growth and generated momentum to support future growth in the coming years as our balance sheet, Founded Entities equity and royalty stakes, and Wholly Owned programs position PureTech with the strength to build substantial value for shareholders in the current environment. This growth is due in large part to (i) significant development and advancement of our Wholly Owned Pipeline and activities initiated or progressed to potentially bring these innovative therapies to market, (ii) continued build out of our executive leadership team and creation of a world-class development organization to support increased operational activities, (iii) our Founded Entities raising in excess of $731 million and progressing their respective business, and (iv) generation of $218.1 million of non-dilutive cash income in 2021 from the sale of equity holdings in Founded Entities. This increase in value, together with management's operational performance at PureTech and within the Wholly Owned Pipeline and Founded Entities, resulted in the Remuneration Committee approving 100% of the target performance goals. In line with our standard approach, the Committee then reviewed the overall performance of the Company and the individual Executive Directors before determining the final bonus payout. The Committee considered operational performance, the overall growth of the business during the year, the extent to which the target performance goals had in some cases been exceeded and the individual contributions of the Executive Directors. As a result of the significant efforts of both Executive Directors in managing the organization in ways not captured by the performance goals set at the beginning of 2021, including taking on additional responsibilities as they managed the transition from the departure of two long-tenured senior leaders with minimal disruption to the business, the Committee determined that a number of additional critical objectives had also been achieved and decided that a bonus equal to 150% of target (or 75% of base salary) was to be awarded to the Executive Directors. The Committee is of the view that this is appropriate in recognizing the Executive Directors' achievements in strengthening the organization and its balance sheet in 2021 and entirely in line with the operational performance delivered during the year and the overall growth of the business. See highlights of 2021 on pages 1 to 9.

In relation to the PSP, PureTech's performance over the last three financial years was very strong with an increase in share price from 172 pence to 292 pence from December 31, 2018 to December 31, 2021 representing an average annual total shareholder return during the period of approximately 23.8%, significantly above the maximum target of 15% per annum set in the PSP awards. This, along with our relative total shareholder return performance and strong strategic performance over the three-year performance period, resulted in the vesting of 95.8 percent of the PSP awards granted to the executive management team, including the two Executive Directors, in 2019.

For the year ended December 31, 2021, the Committee believes the Remuneration Policy operated as intended and that remuneration outcomes are appropriate, taking into account remuneration outcomes throughout the business, company performance and the stakeholder experience. As mentioned above, the Committee determined that the final payout under the annual bonus plan for 2021 to the Executive Directors should be increased from 100% of target to 150% of target, reflective of the achievements during the year, and the individual contributions of the Executive Directors. No discretion has been exercised in relation to the PSP vesting outcome.

The year ahead

For 2022, the following key decisions have been made in relation to how the Policy will be implemented:

- Base salaries for the Executive Directors will be increased by 6 percent in line with the average increase for the general workforce taking into consideration a number of factors, including the current inflationary pressures in the United States;
- The annual bonus target and maximum will remain at 50 percent and 100 percent of base salary, respectively; and
- The grants of PSP awards in 2022 will be at levels of 500 percent of base salary for the Chief Executive Officer and 250 percent of salary for the President. These grant levels are lower than the maximum permitted under the Directors' Remuneration Policy, and lower than the grant levels in 2021. This takes into account the current share price and the resulting impact on the number of shares underlying each award.

Closing comments

The Committee is comfortable that the operation of the Policy for 2021 has demonstrated a robust link between performance and reward. The Committee believes the proposed operation of the Policy for 2022 is appropriate and takes into account the wider stakeholder experience.

The Committee looks forward to shareholders' support for the shareholder resolution for this Annual Statement and the Annual Report on Remuneration at the 2022 Annual General Meeting.

Directors' Remuneration Policy

This part of the Directors' Remuneration Report sets out the Remuneration Policy for the Executive Directors and has been prepared in accordance with the provisions of the Companies Act 2006, The Large and Medium Sized Companies and Groups (Accounts and Reports) (Amendment) Regulations 2008 and the subsequent amendments, and the UK Listing Authority Listing Rules. In addition, the report has been prepared on a "comply or explain" basis with regard to the UK Corporate Governance Code 2018.

This Directors' Remuneration Policy was approved by a binding shareholder vote at the Company's AGM on May 27, 2021. Unless the Company proposes changes to the policy, it will apply for a period of three years from that date. The approved Remuneration Policy can be found in the Director's Remuneration Report of our 2020 Annual Report and Accounts available in the Investor Relations portion of our website at www.puretechhealth.com.

All tables within this Directors' Remuneration Policy section are audited under the International Standards on Auditing (UK) ("ISAs (UK)") unless otherwise noted.

Decision making process for determination, review and implementation of Directors' Remuneration Policy

The Committee reviews the Policy and its operation to ensure it continues to support and align to the business strategy and appropriately reward the Executive Directors and takes into account relevant market practice, regulation and governance developments, institutional investor views and the views of our shareholders. The Committee also has regard to the remuneration arrangements, policies and practices of the workforce as a whole and takes this into account when reviewing Executive Director pay.

The Policy is reviewed annually by the Committee. If changes are required, a new policy will be put forward to shareholder vote prior to the normal triennial shareholder vote. The Committee consults with shareholders on remuneration proposals and will consider the feedback in finalizing the Policy.

Operation of the Policy is considered annually for the year ahead, including metrics for incentives, weightings and targets. The Committee reviews operation for the prior year and considers whether, in light of the strategy, changes are required for the year ahead or if remuneration remains appropriate for the year ahead. Shareholders' views may be sought depending on the changes proposed.

Element	How component supports corporate strategy	Operation	Maximum	Performance targets and recovery provisions
Base salary	To recognize the market value of the employee and the role.	Normally reviewed annually. Salaries are benchmarked periodically primarily against biotech, pharmaceutical and specialty finance companies listed in the U.S. and UK. The committee also considers UK-listed general industry companies of similar size to PureTech as a secondary point of reference.	There is no prescribed maximum base salary or annual salary increase. The Committee is guided by the general increase for the broader employee population but may decide to award a lower increase for Executive Directors or indeed exceed this to recognize, for example, an increase in the scale, scope or responsibility of the role and/or to take account relevant market movements. Current salary levels are set out in the Annual Report on Remuneration.	Not applicable.
Pension	To provide a market competitive level of contribution to pension.	The company operates a 401k Plan for its U.S. Executive Directors. The operation of the Plan is in line with the operation for all other employees.	Under the 401k Plan, Company contributions are capped at the lower of 3 percent of base salary or the maximum permitted by the U.S. IRS ($19,500 for 2021).	Not applicable.
Benefits	To provide a market competitive level of benefits.	Includes: private medical and dental cover, disability, life insurance. Additional benefits may also be provided in certain circumstances, such as those provided to all employees.	Cost paid by the company.	Not applicable.

Element	How component supports corporate strategy	Operation	Maximum	Performance targets and recovery provisions
Annual Bonus Plan (ABP)	To drive and reward annual performance of individuals, teams and PureTech.	Based on performance during the relevant financial year. Paid in cash. The Committee has discretion to adjust payout levels if it considers the formulaic outcome inappropriate taking into account the underlying financial performance of the Company, share price performance, the investment return to shareholders during the year, and such other factors as it considers appropriate.	Up to 100 percent of base salary.	Performance period: Normally one year. Payments are normally based on a scorecard of strategic and/or financial measures. Up to 0 percent of salary payable for threshold performance, 50 percent of base salary normally payable for the achievement of 'target' performance and 100 percent of base salary payable for the achievement of stretch performance. Recovery and withholding provisions are in place.
Long-term incentives	To drive and reward our sustained performance and to align the interests with those of shareholders.	The Company can make long-term incentive awards with the following features: • performance shares. • vesting is dependent on the satisfaction of performance targets and continued service. • performance and vesting periods are normally three years. Awards granted from 2019 onwards will be subject to a two-year post-vesting holding period during which vested shares cannot be sold other than to settle tax. This post-vesting period continues post-cessation of employment. The Committee also has the discretion to adjust vesting levels of performance-related awards to override formulaic outcomes, taking into account similar factors as apply in relation to annual bonus awards, but by reference to the performance period.	600 percent of salary for the Chief Executive Officer, 300 percent of base salary for the other Executive Directors. Participants may benefit from the value of dividends paid over the vesting period to the extent that awards vest. This benefit is delivered in the form of cash or additional shares at the time that awards vest.	Performance period: Normally three years. Up to 25 percent of an award vests at threshold performance (0 percent vests below this), increasing to 100 percent pro-rata for maximum performance. Normally at least half of any award will be measured against TSR targets with the remainder measured against relevant financial or strategic measures. Recovery and withholding provisions are in place.
Share ownership/ Holding Period	Further aligns executives with investors, while encouraging employee share ownership.	The Committee requires that Executive Directors who participate in a long-term incentive plan operated by the Company retain half of the net shares vesting under any long-term incentive plan until a shareholding requirement is met.	Minimum of 400 percent of base salary for the Chief Executive Officer and a minimum of 200 percent of base salary for the other Executive Directors.	None.
Post-cessation holding period	Aligns executives with investors and promotes long-term decision making	Executive Directors must hold shares for two years after the date of termination of their employment.	Lower of (i) 400 percent of base salary for the Chief Executive Officer and 200 percent of base salary for the other Executive Directors and (ii) the Executive Director's shareholding at the date that notice is served.	None.

Element	How component supports corporate strategy	Operation	Maximum	Performance targets and recovery provisions
Non-Executive Directors	To provide fee levels and structure reflecting time commitments and responsibilities of each role, in line with those provided by similarly-sized companies and companies operating in our sector.	Remuneration provided to Non-Executive Directors is operated in line with the terms set out in the Articles of Association. Cash fees, normally paid on a quarterly basis, are comprised of the following elements: • Base fee. • Additional fees. Beginning in 2021, a portion of the compensation to our Non-Executive Directors was in the form of our ordinary shares. Additional remuneration is payable for additional services to PureTech such as the Chairship of a Committee or membership on a Committee. Additional remuneration is also payable for services provided beyond those services traditionally provided as a director, and can be provided for a material increase in time commitment. Fees are reviewed annually and take into account: • the median level of fees for similar positions in the market; and • the time commitment each Non-Executive Director makes to us. Taxable benefits may be provided and may be grossed up where appropriate.	Any remuneration provided to a Non-Executive Director will be in line with the limits set out in the Articles of Association.	None.

Notes:

1 In the event that the Company elects any non-U.S. Executive Directors, the 401k Plan may not be an appropriate pension arrangement. In such cases an alternative pension arrangement may be offered. Any such arrangement would not be higher than the pension rate operated for the majority of employees in that jurisdiction.

2 For those below Board level, a lower annual bonus opportunity and PSP award size may apply. In general, these differences arise from the development of remuneration arrangements that are market competitive for the various categories of individuals, together with the fact that remuneration of the Executive Directors and senior executives typically has a greater emphasis on performance-related pay.

3 The choice of the performance metrics for the annual bonus scheme reflects the Committee's belief that incentive compensation should be appropriately challenging and linked to the delivery of the Company's strategy. Further information on the choice of performance measures and targets is set out in the Annual Report on Remuneration.

4 The performance conditions applicable to the PSP (see Annual Report on Remuneration) are selected by the Remuneration Committee on the basis that they reward the delivery of long-term returns to shareholders and are consistent with the Company's objective of delivering superior levels of long-term value to shareholders while providing the Company with tools to successfully recruit and retain employees in the U.S.

5 For the avoidance of doubt, the Company reserves the right to honour any commitments entered into in the past with current or former Directors (such as the vesting/exercise of share awards) notwithstanding that these may not be in line with this Remuneration Policy. Details of any payments to former Directors will be set out in the Annual Report on Remuneration as they arise.

Recovery and withholding provisions

Recovery and withholding provisions (''clawback and malus'') may be operated at the discretion of the Remuneration Committee in respect of awards granted under the Performance Share Plan and in certain circumstances under the Annual Bonus Plan (including where there has been a material misstatement of accounts, or in the event of fraud, gross misconduct or conduct having a materially detrimental effect on the Company's reputation).

The issue giving rise to the recovery and withholding must be discovered within three years of vesting and there is flexibility to recover overpayments by withholding future incentive payments and recovering the amount directly from the employee.

Discretions in the policy

To ensure the efficient administration of the variable incentive plans outlined above, the Committee will apply certain operational discretions. These include the following:

- selecting the participants in the plans on an annual basis;
- determining the timing of grants of awards and/or payments;
- determining the quantum of awards and/or payments (within the limits set out in the Policy table above);
- reviewing performance against LTI performance metrics;
- determining the extent of vesting based on the assessment of performance;
- making the appropriate adjustments required in certain circumstances, for instance for changes in capital structure;
- deciding how to settle awards made under the plans, e.g. in cash, shares, nil-cost options or as otherwise permitted under the plan rules;
- overriding formulaic outcomes of incentive plans if determined by the Committee not to be reflective of company performance;

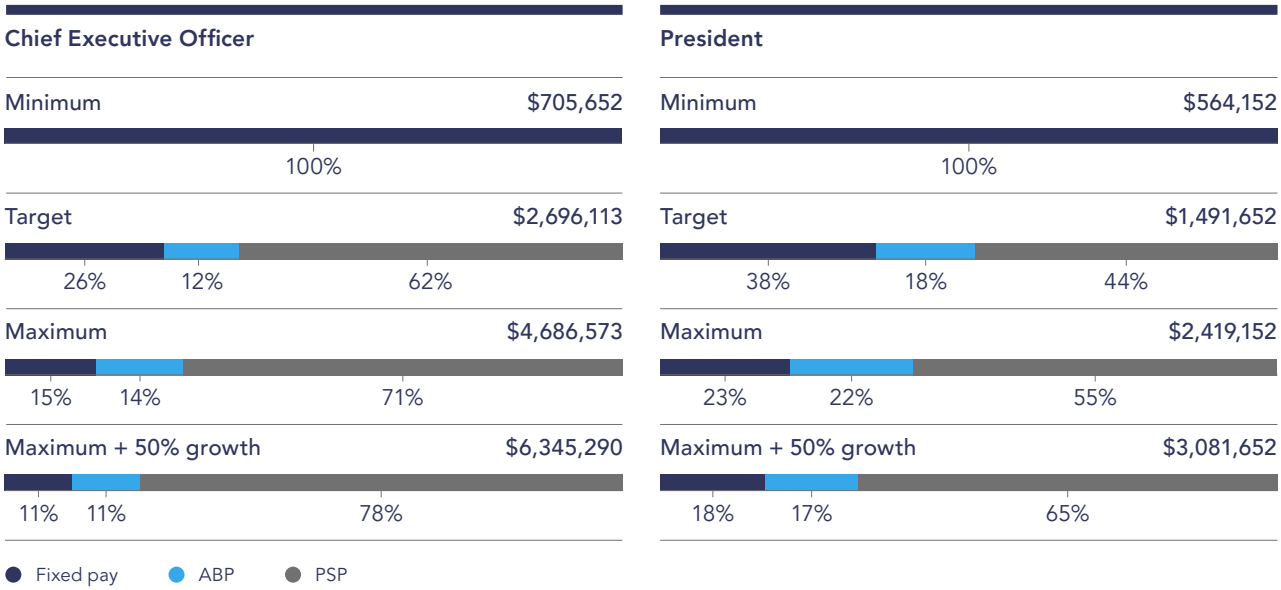
- determining "good leaver" status for incentive plan purposes and applying the appropriate treatment; further details on the discretion applicable in relation to leavers are set out on page 137;
- undertaking the annual review of weighting of performance measures and setting targets for the annual bonus plan and other incentive schemes, where applicable, from year to year; and
- discretion, in the event of a change in control of the Company, to determine that time pro-rating shall not apply to outstanding awards.

If an event occurs which results in the annual bonus plan or PSP performance conditions and/or targets being deemed no longer appropriate (e.g. material acquisition or divestment), the Committee will have the ability to adjust appropriately the measures and/or targets and alter weightings, provided that the revised conditions are not materially less challenging than the original conditions.

Reward scenarios

The charts below show how the composition of 2022 remuneration for the Chief Executive Officer and the President varies at different levels of performance under the Policy set out above, as a percentage of total remuneration opportunity and as a total value.

Executive Director compensation (unaudited)



Notes:

1 The minimum performance scenario comprises the fixed elements of remuneration only, including:
- Salary for FY2022 as set out in the Annual Report on Remuneration.
- Pension in line with policy and benefits as disclosed for FY2021 in the Annual Report on Remuneration.

2 The On-Target level of bonus is taken to be 50 percent of the maximum bonus opportunity (50 percent of salary), and the On-Target level of PSP vesting is assumed to be 50 percent of the face value of the PSP award (i.e. 250 percent of base salary for the CEO and 125 percent of base salary for the President). These values are included in addition to the components/values of Minimum remuneration.

3 Maximum assumes full bonus pay-out (100 percent of base salary only) and the full face value of the proposed PSP awards (i.e. 500 percent of base salary for the CEO and 250 percent of base salary for the President), in addition to fixed components of Minimum remuneration.

4 No share price growth has been factored into the calculations of minimum, target and maximum compensation. An additional maximum scenario has been shown which assumes 50% share price appreciation for the PSP during the performance period.

Approach to recruitment and promotions

The remuneration package for a new Executive Director would be set in accordance with the terms of the Company's prevailing approved Remuneration Policy at the time of appointment and take into account the skills and experience of the individual, the market rate for a candidate of that experience and the importance of securing the relevant individual.

Salary would be provided at such a level as required to attract the most appropriate candidate and may be set initially at or above mid-market level.

Additionally, salary may be provided at a below mid-market level on the basis that it may progress towards the mid-market level once expertise and performance has been proven and sustained. The annual bonus and long-term incentive awards would be limited in line with the policy. Depending on the timing of the appointment, the Committee may deem it appropriate to set annual bonus performance conditions for such appointee that are different than those applicable to the incumbent Executive Directors. A PSP award can be made shortly following an appointment.

In addition, the Committee may offer additional cash and/or share-based elements to replace deferred or incentive pay forfeited by an executive leaving a previous employer if required in order to facilitate, in exceptional circumstances, the recruitment of the relevant individual. It would seek to ensure, where possible, that these awards would be consistent with awards forfeited in terms of vesting periods, expected value, performance conditions and delivery mechanism.

For appointment of an Executive Director who was employed by the Company prior to the appointment, any variable pay element awarded in respect of the prior role may be allowed to pay out according to its terms. In addition, any other ongoing remuneration obligations existing prior to appointment may continue.

For any Executive Director appointment, the Committee may agree that the Company will meet certain relocation and/or incidental expenses as appropriate.

Service contracts

Executive Directors' service contracts do not provide for liquidated damages, longer periods of notice on a change of control of the Company or additional compensation on an Executive Director's cessation of employment with us, except as discussed below.

The Committee's Policy is to offer service contracts for Executive Directors with notice periods of no more than 12 months, and typically between 60 to 180 days.

Service contracts provide for severance pay following termination in the case that employment is terminated by the Company without 'cause', or by the employee for 'good reason'. In this case severance pay as set out in the contract is no greater than 12-months' base salary and is aligned to the duration of any restrictive covenants placed on the employee. Service contracts may also provide for the continuation of benefits but for no longer than a 12-month period post termination.

Service contracts also provide for the payment of international tax in non-U.S. jurisdictions if applicable to the Executive Director. They also can provide for garden leave and, if required by applicable law, the recovery and withholding of incentive payments.

Service contracts are available for inspection at the company's registered office.

Policy on termination of employment

The Policy on termination is that the Company does not make payments beyond its contractual obligations and the commitments entered into as part of any incentive plan operated by the Company. In addition, Executive Directors will be expected to mitigate their loss. The Committee ensures that there have been no unjustified payments for failure.

An Executive Director may be eligible for an annual bonus payment for the final year in which that Director served as an employee, provided that they are deemed to be a 'good leaver'. If so, any such annual bonus payment will be subject to performance testing and a pro-rata reduction will normally be applied based on the time served during the relevant financial year.

The default treatment for any share-based entitlements under the PSP is that any unvested outstanding awards lapse on cessation of employment. However, in certain prescribed circumstances, or at the discretion of the Remuneration Committee, 'good leaver' status can be applied. In these circumstances, a participant's awards will vest subject to the satisfaction of the relevant performance criteria and, ordinarily, on a time pro-rated basis, with the balance of the awards lapsing. The two-year post vest holding period will usually continue to apply. The Committee has discretion to permit the early vesting at the date of cessation of employment, again based on performance and ordinarily on a time pro-rated basis.

In addition, the Company can pay for any administrative expenses, legal expenses or outplacement services arising from the termination where considered appropriate.

External appointments

The Board can allow Executive Directors to accept appropriate outside commercial Non-Executive Director appointments provided that the duties and time commitment required are compatible with their duties and time commitment as Executive Directors.

Non-Executive Directors

Non-Executive Directors are appointed as a Non-Executive Director of the Company by a letter of appointment. These letters usually provide for a notice period of one month from the Company and the Non-Executive Director prior to termination.

Consideration of shareholder views

The Committee will carefully consider shareholder feedback received in relation to the AGM each year. This feedback, plus any additional feedback received during any meetings from time to time, is then considered as part of the annual review of the Remuneration Policy.

The Company will seek to engage directly with major shareholders and their representative bodies should any material changes be proposed to the Remuneration Policy or its implementation. Details of votes cast for and against the resolution to approve the prior year's remuneration report and any matters discussed with shareholders during the year will be set out in the Annual Report on Remuneration. The Company consulted with shareholders in 2021, as referenced on page 131, in relation to the proposed changes to the Remuneration Policy and we were pleased to receive support from those consulted.

Consideration of our employment conditions generally

To ensure a coherent cascade of the Remuneration Policy throughout the organization, no element of remuneration is operated solely for Executive Directors and all elements of remuneration provided to the Executive Directors are generally operated for other employees, including participation in stock-based incentive plans. In addition, the Committee considers the general base salary increase for the broader employee population when determining the annual salary increases for the Executive Directors. The Remuneration Committee has general responsibility for determining pay for senior management as well as Executive Directors. Employees (other than senior executives) have not been consulted in respect of the design of our Remuneration Policy, although the Committee will keep this under review.

Annual Report on Remuneration

Implementation of the Remuneration Policy for the year ending December 31, 2022

All tables within the Annual Report on Remuneration are audited under the International Standards on Auditing (UK) ("ISAs (UK)") unless otherwise noted.

Base salary

The Committee reviewed the base salary levels for the Executive Directors in early 2022 and an increase of 6 percent was awarded. This increase was in line with the increase for the general workforce, which was largely driven by cost of living considerations in the US.

		2021 Base salary	**2022 Base salary**
Daphne Zohar	Chief Executive Officer	$625,931	**$663,487**
Bharatt Chowrira	President, Chief Business, Legal and Operating Officer, Corporate Secretary ("President")	$500,000	**$530,000**

Pension

We will continue to contribute under the 401k Plan subject to the maximum set out in the Policy table.

Benefits

Benefits provided will continue to include private medical, disability and dental cover.

Annual bonus

For 2022, the operation of the annual bonus plan will be similar to that operated in 2021. The maximum annual bonus will continue to be 100 percent of base salary for all Executive Directors. The 2022 annual bonus will be based on clinical development milestones and internal program development, financial and strategic measures, and development of new strategic and investor relationships. The performance metrics and targets will be disclosed in the FY2022 Annual Report and Accounts.

Long-term incentives

Awards under the PSP will be made to the Executive Directors in 2022. The Chief Executive Officer will receive a PSP award with a face value of 500 percent of base salary, and the President will receive an award with a face value of 250 percent of base salary. These grant levels are lower than the maximum permitted under the Directors' Remuneration Policy, and lower than the grant levels in 2021. This takes into account the fall in the share price since the grant of the 2021 awards and the resulting impact on the number of shares underlying each award.

The PSP awards will be subject to the performance conditions described below. As a clinical-stage therapeutics company, the Company believes that TSR is an appropriate and objective measure of the Company's performance. In addition, measuring TSR on both an absolute and relative basis rewards our management team for absolute value creation for our shareholders whilst also incentivizing outperformance of the market. To provide a balance to the TSR performance conditions that is more directly based on Management's long term strategic performance, TSR is complemented by measures linked to strategic delivery. There will be a robust assessment of the achievement of the strategic targets over the three year period with full disclosure in the Directors' Remuneration Report following the end of the performance period.

Further detail of the performance conditions is set out below:

- 40 percent of the shares under award will vest based on the achievement of absolute TSR targets.
- 20 percent of the shares under award will vest based on the achievement of a relative TSR performance condition, 10 percent each against two benchmarks (explained below).
- 40 percent of the shares under award will vest based on the achievement of strategic targets.

The minimum performance target for the absolute TSR portion of the award will be TSR equal to 7 percent per annum, whilst the maximum target will be TSR equal to 15 percent per annum. Relative TSR will be measured against the constituent companies in the FTSE 250 Index (excluding Investment Trusts) and the MSCI Europe Health Care Index (for 10 percent of the award, respectively). The minimum performance target will be achievement of TSR equal to the median company in the Index and the maximum performance target will be achievement of upper quartile TSR performance. 25 percent of each element of the TSR targets will vest for threshold performance. Strategic measures will be based on the achievement of milestones and other qualitative measures of performance over the performance period. Strategic targets will be set at the outset based on financial achievements, including monetization of Founded Entities, clinical development progress, product pipeline growth, operational excellence and other shareholder value enhancing metrics in line with our strategic plan. Full disclosure of the measures, weightings and strategic targets will be made retrospectively.

The Committee believes that this combination of measures is appropriate. TSR measures the success of our management team in identifying and developing new therapeutics whilst strategic targets help incentivize our management team through the stages which ultimately result in successful therapeutics.

Non-Executive Directors

Fees for our Board of Directors were reviewed for 2022 and remain unchanged from 2021.

	FY2021 and FY2022
Chair fee	**$125,000**
Basic fee	**$75,000**
Equity-based Component	**$50,000**
Additional fees:	
Chair of a committee	**$10,000**
Membership of a committee	**$5,000**
Membership of a subsidiary board	**$0 to $10,000**

As our Board of Directors consists of leading experts with the experience of successfully developing technologies and bringing them to market, this gives rise to the possibility that the intellectual property we seek to acquire has been developed by one of our Non-Executive Directors and/or that our Non-Executive Directors provide technical or otherwise specialized advisory services to the Company above and beyond the services typically provided by a Non-Executive Director. In such exceptional circumstances, our Remuneration Policy provides us with the flexibility to remunerate them with equity in the relevant subsidiary company as we would any other inventor of the intellectual property or provider of technical advisory services. This practice is in line with other companies in the life sciences sector. If the Company is unable to offer market-competitive remuneration in these circumstances, it risks forfeiting opportunities to obtain intellectual property developed by our Non-Executive Directors and/or foregoing valuable advisory services. The Company believes foregoing such intellectual property and/or advisory services would not be in the long-term interest of our shareholders. Accordingly, subsidiary equity grants may be made to Non-Executive Directors upon the occurrence of the exceptional circumstances set out above.

Remuneration for the year ended December 31, 2021

Single total figure of remuneration for each Director (audited)

The table below sets out remuneration paid in relation to the 2021 financial year with a comparative figure for the 2020 financial year. There were no exercises of share options by Executive Directors or Non-Executive Directors in either of the 2021 or 2020 financial years.

		2021 and 2020 Remuneration								
	Year	Basic Salary/ Fees	Benefits[1]	Annual Bonus Plan	Performance Share Plan (Vested)[2]	Pension	Other payments[3]	Total Remuneration	Total Variable	Total Fixed
Executive Directors										
Daphne Zohar	**2021**	**$625,931**	**$33,465**	**$469,448**	**$2,693,882**	**$8,700**	**—**	**$3,831,426**	**$3,163,330**	**$668,096**
	2020	$607,700	$31,069	$607,700	$5,679,700[7]	$8,550	$260,122	$7,194,841	$6,287,400	$907,441
Bharatt Chowrira[4]	**2021**	**$500,000**	**$25,452**	**$375,000**	**$511,046**	**$8,700**	**—**	**$1,420,198**	**$886,046**	**$534,152**
Stephen Muniz[5]	**2021**	**$164,786**	**$11,396**	**—**	**—**	**$8,700**	**—**	**$184,882**	**—**	**$184,882**
	2020	$422,300	$28,919	$422,300	$1,901,101[7]	$8,550		$2,783,986	$2,323,401	$459,769
Non-Executive Directors										
Raju Kucherlapati	**2021**	**$145,000[8]**	**—**	**—**	**—**	**—**		**$145,000**		**$145,000**
	2020	$105,000	—	—	—	—		$105,000		$105,000
John LaMattina	**2021**	**$145,000[8]**	**—**	**—**	**—**	**—**		**$145,000**		**$145,000**
	2020	$125,000	—	—	—	—		$125,000		$125,000
Robert Langer	**2021**	**$145,000[8]**	**—**	**—**	**—**	**—**		**$145,000**		**$145,000**
	2020	$125,000	—	—	—	—		$125,000		$125,000
Kiran Mazumdar-Shaw[6]	**2021**	**$135,000[8]**	**—**	**—**	**—**	**—**		**$135,000**		**$135,000**
	2020	$21,250	—	—	—	—		$21,250		$21,250
Dame Marjorie Scardino	**2021**	**$140,000[8]**	**—**	**—**	**—**	**—**		**$140,000**		**$140,000**
	2020	$90,000	—	—	—	—		$90,000		$90,000
Christopher Viehbacher	**2021**	**$195,000[8]**	**—**	**—**	**—**	**—**		**$195,000**		**$195,000**
	2020	$155,000	—	—	—	—		$155,000		$155,000
TOTAL	**2021**	**$2,195,717**	**$70,313**	**$844,448**	**$3,204,928**	**$26,100**	**—**	**$6,341,506**	**$4,049,376**	**$2,292,130**
TOTAL	2020	$1,651,250	$59,988	$1,030,000	$7,580,801	$17,100	$260,122	$10,600,077	$8,610,801	$1,988,460

Notes:

1 Benefits comprise the following elements: private medical, disability and dental cover and parking.

2 The shares underlying the vested 2019 Performance Share Plan awards will be issued after the finalisation of this report. As a result, the share price on the date of issuance is not known at the date of this report and the figures shown above for the PSP awards have been valued using a share price of £3.236875, which was the average share price during the last three months of 2021, and an exchange rate of GBP 1 : USD 1.34809697, which was the average exchange rate over the last three months of 2021.

3 Other payments represent a one-time reimbursement to Ms. Zohar for costs associated with converting certain of her ordinary shares into ADSs, as required by Nasdaq prior to our listing on Nasdaq in November 2020.

4 Dr. Chowrira joined the Board in February 2021.

5 Mr. Muniz retired from the Board in May 2021.

6 Ms. Mazumdar-Shaw joined the Board in September 2020.

7 These amounts have been updated from those listed in the 2020 Annual Report and Accounts to reflect the actual values paid, which was not known at the date of publication of the 2020 Annual Report and Accounts.

8 These amounts include grants of share based remuneration on July 21, 2021 in the form 11,190 time-vesting restricted stock units with a face value of $50,000.

Annual bonus outcome for 2021

For the 2021 annual bonus, targets were set for a balanced scorecard at the beginning of the year. The 2021 targets were focused on (i) internal program development goals designed to incentivize the team to continue development of the Company's Wholly Owned Pipeline, generate valuable clinical data in support of the Company's programs and create innovative programs, (ii) strategic goals designed to incentivize the team to complete important deals and execute strategic partnerships, (iii) monetization and investor related goals designed to incentivize the team to generate non-dilutive cash and achieve enhanced analyst coverage of the Company's stock to support shareholder value generation, and (iv) Controlled Founded Entity program development goals designed to incentivize the team to take steps necessary to progress towards the potential commercial launch of therapeutics at our Founded Entities. In addition, the Remuneration Committee took into account other goals and other achievements by the management team in setting final achievement attainment and fixing bonus payouts. The table below sets out the performance assessment and associated bonus outcomes:

Target Goals – Maximum 100 percent Achievement

Performance Measures Category	Achievement	Percentage of Target Attained
Internal Program Development	The Internal Program Development Goals were 80% achieved in 2021. The management team's performance resulted in an achievement outcome of 40 percent out of a pre-specified cap of 50 percent for this category of the goals. A description of performance in 2021 is set out below: The Company's LYT 100 Long COVID study was fully enrolled, multiple clinical studies to demonstrate improved tolerability as compared to pirfenidone were completed, early-stage data was generated for LYT 200, the first human dose of LYT 300 was administered, proof of concept was achieved in rodents for the Orasome platform, and additional early-stage work was completed on certain other programs.	40%
Strategic Goals	The Strategic Goals were achieved in 2021. The management team's performance resulted in an achievement outcome of 20 percent which was equal to the pre-specified cap of 20 percent for this category of the goals. A description of performance in 2021 is set out below: The Company completed the acquisition of Alivio Therapeutics that added LYT 500 to the Company's Wholly Owned Pipeline, Gelesis announced that It would go public via a SPAC transaction (which closed In the January post-period), Akili progressed towards going public via a SPAC transaction (which was announced In the January post-period), Vedanta secured over $68 million in financing, and Karuna secured a partnership with Zai Lab with $35 million in upfront licensing fees and future potential milestone payments.	20%
Monetization and Investor Related Goals	The Monetization and Investor Related Goals were achieved in 2021. The management team's performance resulted in an achievement outcome of 20 percent which was equal to the pre-specified cap of 20 percent for this category of the goals. A description of performance in 2021 is set out below: The Company had $218 million of cash income in 2021 from the sale of equity holdings, and added a new analyst from a major investment bank.	20%
Controlled Founded Entity Program Development	The Controlled Entity Program Development Goals were achieved in 2021. The management team's performance resulted in an achievement outcome of 10 percent which was equal to the cap of 10 percent for this category of the goals. A description of performance in 2021 is set out below: Vedanta's phase 1 and 2 studies were completed with the phase 2 study for VE303 achieving its primary endpoint.	40%
Other Achievements	The management team evidenced further exceptional performance as described below: The Company recruited a seasoned chief medical officer and built a world-class development organization, operated within the pre-set budget, managed operations during the COVID-19 pandemic to execute all programs in accordance with the operating plan and achieved all core objectives, observed strict COVID-related protocols to minimize employee exposure and achieved a 100% vaccination rate among its employees, and managed the transition associated with two long-tenured senior executives with minimal disruption to the business.	10%
Pre-Specified Maximum Total		**100%**

Accordingly, determined that the Company had achieved 100 percent of its target goals for 2021.

Each of the above target categories are subject to maximum percentage achievement limits capped at 100 percent of the target bonus (i.e. 50 percent of salary). Payments beyond the target are determined by the Remuneration Committee taking into account the extent target goals have been exceeded, the overall quality of underlying performance, value created for shareholders and other relevant factors. In this case, the Company performed above the target maximum goals, including with respect to the other achievements described above related to operational performance and contribution to overall growth of the business during the year. The Committee also considered the additional responsibilities taken on by the Executive Directors during the year following the departure of certain senior executives and the need to ensure an appropriate level of continuity. In light of these achievements, the Committee determined that payouts at 150 percent of target (i.e. 75 percent of salary) are appropriate for the Executive Directors as explained earlier in this report. The Committee believes that such a bonus award is appropriate to reward and retain top management when such extraordinary performance is achieved.

Long-term incentive awards vesting in respect of the year (unaudited)

The 2019 PSP awards granted on December 20, 2019 were subject to three-year performance conditions covering the period from January 1, 2019 to December 31, 2021. Following an assessment of the performance conditions, the Remuneration Committee determined that the awards will vest at 95.8 percent of the maximum. Stephen Muniz's shares lapsed following his retirement in May 2021.

	Scheme	Basis of award granted	Shares awarded	Shares vested	Shares lapsed	Value of vested awards[1,2]
Daphne Zohar	PSP 2019	400% of salary	644,668	617,350	27,318	$2,693,882
Bharatt Chowrira	PSP 2019	100% of salary	122,924	117,715	5,209	$511,046

1 Shares have been valued using a share price of £3.236875, which was the average share price during the last three months of 2021, and an exchange rate of GBP 1 : USD 1.34809697, which was the average exchange rate over the last three months of 2021.

2 The value of the awards attributable to share price appreciation is $433,887 for Daphne Zohar and $80,115 for Bharatt Chowrira.

The outcome of the performance condition relating to these awards is set out below (unaudited):

Measure and weighting	Threshold	Maximum	Achievement	Vesting (% of each element)
Absolute TSR (50%)	7% p.a.	15% p.a.	23.8% p.a.	100%
Total return against FTSE Small Cap Index (12.5%)	At or above median	Upper quartile	83rd percentile	100%
Total return against MSCI Euro Healthcare Index (12.5%)	At or above median	Upper quartile	63rd percentile	66.4%
Strategic measures (25%)	See description below			100%

The strategic measures over the three-year period were focused on (i) financial goals (59 percent), (ii) clinical development goals (34 percent), and (iii) operational excellence (7 percent). The financial achievements resulting in satisfaction of 59 percent of the vesting of the strategic measures included obtaining $563 million for PureTech by monetizing certain Founded Entity equity, the closing of initial public offerings of two Founded Entities and the announcement of two SPAC transactions for Founded Entities, the execution of several partnership agreements which brought in non-dilutive funding, the raising of more than $1.58 billion into the Company's Founded Entities and the completion of PureTech's listing on the Nasdaq Global Market. The clinical development achievements resulting in satisfaction of 34 percent of the vesting of the strategic measures included the successful completion of several Phase 1 clinical studies for LYT-100 and the completion of enrollment In LYT-100 Long COVID phase 2 study, the advancement of other programs within our Wholly Owned Pipeline, the successful completion of Phase 2 clinical studies for the KarXT program, the completion of a Phase 2 clinical study for the VE303 program and the completion of Phase 1 clinical studies for the VE202 and VE416 programs, and successfully having two programs cleared for marketing by the U.S. Food and Drug Administration. The operational excellence achievements resulting in satisfaction of 7 percent of the vesting of the strategic measures include the operation of the Company's programs within projected timelines and budgets, successfully managing operations through the COVID-19 pandemic, building out a world-class development organization, the in-licensing and creation of new programs, the issuance of certain intellectual property, the advancement of certain pre-clinical programs, and the publication of validating data in top tier peer-reviewed academic journals.

Long-term incentive awards granted during the year (audited)

The following long-term Incentive awards were granted to Executive Directors during 2021:

	Scheme	Basis of award granted	Shares awarded (as conditional award of shares)	Share price at date of grant[1]	Face value of award	% of face value vesting at threshold performance	Vesting determined by performance over
Daphne Zohar	PSP 2021	600% of salary	683,652	282.33 pence	$2,430,800	20%	Three financial years to December 31, 2023
Bharatt Chowrira	PSP 2021	300% of salary	335,687	326.83 pence	$1,500,000	20%	

1 The share price at the date of grant is based on the 3-day average closing price immediately prior to the grant of the award.

The PSP awards granted in 2021 are subject to (i) achievement of absolute TSR targets (40 percent of the awards), (ii) achievement of TSR targets as compared to TSR performance of the constituent companies in the FTSE 250 Index (excluding Investment Trusts) and the MSCI Europe Health Care Index (20 percent of the awards, 10 percent against each benchmark) and (iii) achievement of targets based on strategic measures (40 percent of the awards), measured over the three year period to December 31, 2023.

The minimum performance target for the absolute TSR portion of the award is TSR equal to 7 percent per annum, whilst the maximum target is TSR equal to 15 percent per annum. The minimum performance target for the relative TSR portion of the award is TSR equal to the median of the index, whilst the maximum target will be TSR equal to the upper quartile of the index. Strategic measures are based on the achievement of project milestones and other qualitative measures of performance. Strategic targets have been set based on financial achievements, including monetization of Founded Entities, clinical development progress, product pipeline growth, operational excellence and other shareholder value enhancing metrics in line with our strategic plan. The Committee believes that this combination of measures and the equal weighting on TSR and strategic objectives is appropriate. TSR measures the success of our management team in identifying and developing new therapeutics whilst strategic targets help incentivize our management team through the stages which ultimately result in successful therapeutics.

Full disclosure of the strategic targets will be made retrospectively.

In addition, each Non-Executive Director was granted share based remuneration on July 21, 2021 in the form of 11,190 time-vesting restricted stock units. The equity awards granted to our Non-Executive Directors vest in their entirety immediately prior to Company's 2022 AGM, provided that the Non-Executive Directors continue their service through such date. This share based element is part of the annual fee for Non-Executive Directors and is not subject to performance (unaudited).

Non-Executive Directors	Shares awarded	Face value of award[1]	Vesting date
Raju Kucherlapati	11,190	$50,000	June 15, 2022
John LaMattina	11,190	$50,000	June 15, 2022
Robert Langer	11,190	$50,000	June 15, 2022
Kiran Mazumdar-Shaw	11,190	$50,000	June 15, 2022
Dame Marjorie Scardino	11,190	$50,000	June 15, 2022
Christopher Viehbacher	11,190	$50,000	June 15, 2022

Payments for Loss of Office (unaudited)

There were no payments for Loss of Office during 2021.

On March 18, 2021 the Company announced that Stephen Muniz would retire from the company and step down from the board on May 17, 2021. He continued to be paid base salary, benefits and pension until May 17, 2021, at which point payments ceased. There was no compensation payable for loss of office, no eligibility for 2021 bonus and all unvested PSP awards lapsed. Vested PSP awards remain subject to any applicable holding period and the post-employment shareholding policy applies, requiring a shareholding worth 200 percent of Mr. Muniz's final base salary level to be retained for two years.

Payments to past Directors (unaudited)

No payments to past Directors were made during 2021.

Directors' shareholdings (audited)

Executive Directors are required to maintain share ownership equal to a minimum of 400 percent of base salary for the Chief Executive Officer (subject to approval of the new policy) and a minimum of 200 percent of base salary for the other Executive Directors. The Chief Executive Officer and President both satisfy this requirement, and neither has disposed of any company shares since the Company's IPO. Post-employment shareholding requirements will apply.

The table below sets out current Directors' shareholdings which are beneficially owned or subject to a performance condition and interests of connected persons.

	Director Shareholdings					
	Total Share Awards not subject to Service Conditions		Share awards subject to performance conditions		Total	
Director	**Dec 31, 2021**	Dec 31, 2020	**Dec 31, 2021**	Dec 31, 2020	**Dec 31, 2021**	Dec 31, 2020
Daphne Zohar[1]	**12,197,307**[2]	12,197,307	**1,524,120**[3]	1,328,320[4]	**13,721,427**	13,525,627
Bharatt Chowrira[5]	**2,213,689**[6]	—	**1,158,902**[7]	—	**3,372,591**	—
Stephen Muniz[8]	**3,096,590**[8]	2,889,499	**—**	461,535	**3,096,590**[8]	3,351,034
Raju Kucherlapati	**2,459,831**	2,459,831	**11,190**[9]	—	**2,471,021**	2,459,831
John LaMattina[10]	**1,513,133**	1,495,332	**11,190**[9]	—	**1,524,323**	1,513,133
Robert Langer[11]	**2,944,134**	2,944,134	**11,190**[9]	—	**2,955,324**	2,944,134
Kiran Mazumdar-Shaw	**—**	—	**11,190**[9]	—	**11,190**	—
Dame Marjorie Scardino	**798,710**[12]	788,710	**11,190**[9]	—	**809,900**	788,710
Chris Viehbacher	**1,045,646**[13]	1,045,646	**11,190**[9]	—	**1,056,836**	1,045,646

1 A portion of Ms. Zohar's shareholding in the Company is indirect. As of December 31, 2020, an aggregate of 8,097,307 ordinary shares and 410,000 ADSs are held by (i) the Zohar Family Trust I, a U.S.-established trust of which Ms. Zohar is a beneficiary and trustee, (ii) the Zohar Family Trust II, a U.S.-established trust of which Ms Zohar is a beneficiary (in the event of her spouse's death) and trustee, (iii) Zohar LLC, a U.S.-established limited liability company, and (iv) directly by Ms. Zohar. Ms. Zohar owns or has a beneficial interest in 100 percent of the share capital of Zohar LLC.

2 ncludes 410,000 ADSs, which are convertible into 4,100,000 ordinary shares. Does not include 617, 350 shares which are issuable pursuant to the RSU award granted to Ms. Zohar covering the financial years 2019, 2020 and 2021 which have vested but not yet been issued.

3 Includes the following RSUs, which are subject to performance conditions: 683,652 (2020) and 840,468 (2021). Does not include 617, 350 shares which are issuable pursuant to the RSU award granted to Ms. Zohar covering the financial years 2019, 2020 and 2021 which have vested but not yet been issued.

4 Includes the following RSUs, which are subject to performance conditions: 644,668 (2019) and 683, 652 (2020).

5 Dr. Chowrira joined the board as an executive director in 2021.

6 Includes 826,189 shares of stock owned by Dr. Chowrira and 1,387,500 vested stock options, none of which have been exercised. Does not include 117,715 shares which are issuable pursuant to the RSU award granted to Dr. Chowrira covering the financial years 2019, 2020 and 2021 which have vested but not yet been issued.

7 Includes the following RSUs, which are subject to performance conditions: 260,715 (2020) and 335, 687 (2021), as well as 562,500 unvested stock options. Does not include 117,715 shares which are issuable pursuant to the RSU award granted to Dr. Chowrira covering the financial years 2019, 2020 and 2021 which have vested but not yet been issued.

8 Mr. Muniz retired on May 17, 2021. The values set forth for Mr. Muniz with reference to 2021 reflect Mr. Muniz's stock ownership immediately following his retirement, at which point Mr. Muniz forfeited any share based awards which had not yet vested.

9 Includes RSUs, which are subject to performance conditions, that were granted in July 2021 and vest immediately prior to the 2022 Annual General Meeting.

10 A portion of Dr. LaMattina's shareholding in the Company is indirect. As of December 31, 2021, an aggregate of 1,513,133 ordinary shares are held by (i) John L LaMattina Revocable Trust, (ii) John L LaMattina 2020-2 GRAT, and (iii) LaMattina Charitable Trust.

11 A portion of Dr. Langer's shareholding in the Company is indirect. As of December 31, 2021, an aggregate of 2,944,134 ordinary shares are held by (i) Langer Family 2020 Trust and (ii) directly by Dr. Langer.

12 Includes 100 ADSs, which are convertible into 1,000 ordinary shares.

13 Includes 2,000 ADSs, which are convertible into 20,000 ordinary shares.

Directors' service contracts (unaudited)

Detail of the service contracts of current Directors is set out below:

Executive Directors	Notice period	Contract date	Maximum potential termination payment	Potential payment on change of control/liquidation
Daphne Zohar	180 days	June 18, 2015	12 months' salary	Nil
Bharatt Chowrira	60 days	March 1, 2017	12 months' salary	Nil

Contracts for the above Executive Directors will continue until terminated by notice either by the Company or the Executive Director. Mr. Muniz terminated his service contract and his notice period ended on May 17, 2021.

Non-Executive Directors	Notice period	Contract date	Contract expiration date
Sharon Barber-Lui	30 days	March 24, 2022	March 24, 2025
Raju Kucherlapati	30 days	June 5, 2021	June 5, 2024
John LaMattina	30 days	June 5, 2021	June 5, 2024
Robert Langer	30 days	June 5, 2021	June 5, 2024
Kiran Mazumdar-Shaw	30 days	September 28, 2020	September 28, 2023
Marjorie Scardino	30 days	June 5, 2021	June 5, 2024
Christopher Viehbacher	30 days	June 5, 2021	June 5, 2024

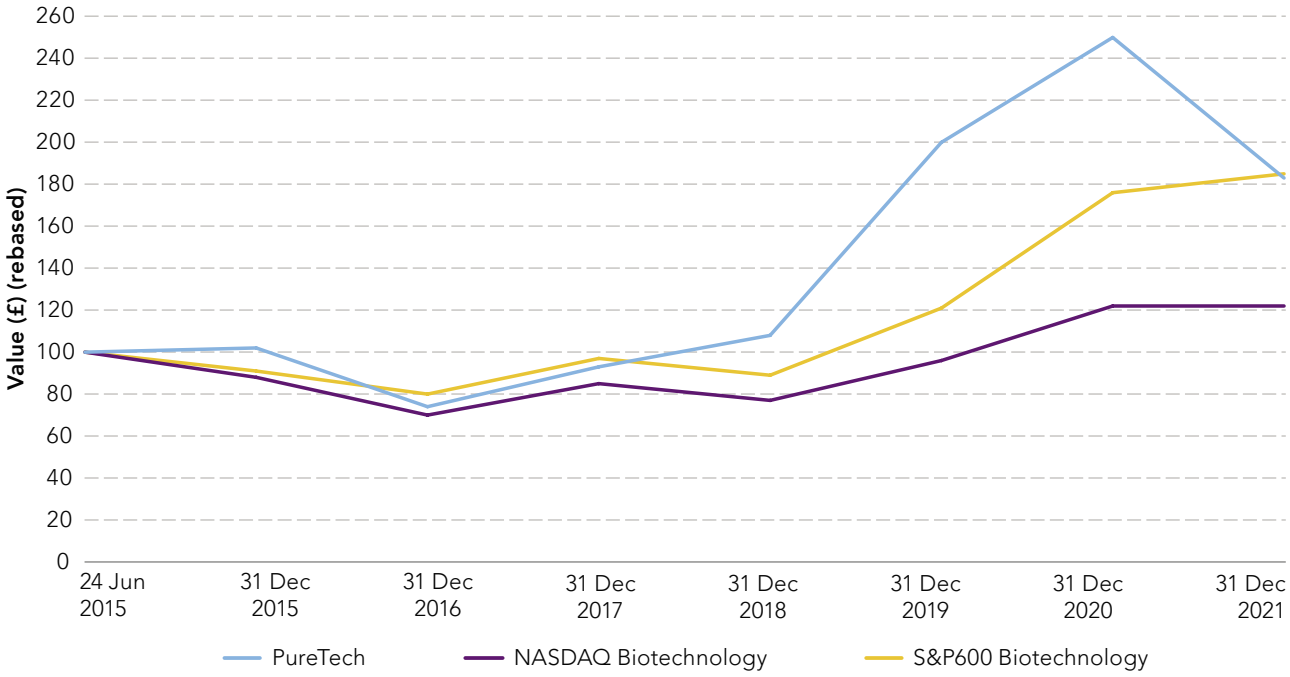
The Company and the Non-Executive Directors listed above intend to enter into new contracts prior to their expiration.

TSR performance graph (unaudited)

The graph shows the Company's performance, measured by total shareholder return (TSR), compared with the Nasdaq Biotechnology Index and S&P600 Biotechnology Index since the Company's IPO. The Committee considers these to be relevant indices for TSR comparison as they are broad-based measures of the performance of the biotechnology industry.

Total shareholder return (unaudited)

Source: Datastream (Thomson Reuters)



This graph shows the value, by December 31, 2021, of £100 invested in PureTech on the date of Admission (June 24, 2015), compared with the value of £100 invested in the Nasdaq Biotechnology and S&P600 Biotechnology indices on the same date.

The other points plotted are the values at intervening financial year-ends.

Chief Executive Officer's Remuneration History (unaudited)

Year	Incumbent	Role	Single figure of total remuneration	Annual bonus pay-out against maximum	PSP Vesting against maximum opportunity
2015	Daphne Zohar	Chief Executive Officer	$955,599	100%	n/a
2016	Daphne Zohar	Chief Executive Officer	$747,634	38.75%	n/a
2017	Daphne Zohar	Chief Executive Officer	$821,898	50%	n/a
2018	Daphne Zohar	Chief Executive Officer	$2,139,870	65%	50%
2019	Daphne Zohar	Chief Executive Officer	$5,783,682	100%	100%
2020	Daphne Zohar	Chief Executive Officer	$7,194,841	100%	100%
2021	**Daphne Zohar**	**Chief Executive Officer**	**$3,831,426**	**75%**	**95.8%**

Percentage change in remuneration of Directors and employees (unaudited)

The table below shows the change in the Directors' remuneration from 2020 to 2021 and 2019 to 2020 compared to the change in remuneration of all of our full-time employees who were employed throughout the same periods:

	2020 to 2021			2019 to 2020		
	Base salary[1]	Benefits	Annual bonus	Base Salary	Benefits	Annual Bonus
Daphne Zohar (CEO)	3%	6%	(23%)	3%	0%	3%
Bharatt Chowrira (President)[2]	N/A	N/A	N/A	N/A	N/A	N/A
Raju Kucherlapati	38.1%	N/A	N/A	11%	N/A	N/A
John LaMattina	16%	N/A	N/A	19%	N/A	N/A
Robert Langer	16%	N/A	N/A	13%	N/A	N/A
Kiran Mazumdar-Shaw[3]	635%	N/A	N/A	N/A	N/A	N/A
Marjorie Scardino	55%	N/A	N/A	0%	N/A	N/A
Christopher Viehbacher	26%	N/A	N/A	45%	N/A	N/A
Employees[4]	9%	7%	1%	8%	16%	14%

1 Base salary amounts for Non-Executive Directors in 2021 include grants of share based remuneration on July 21, 2021 in the form 11,190 time-vesting restricted stock units with a face value of $50,000.
2 Joined the Board effective February 2021.
3 Joined the Board effective September 2020. As a result, the increase in base salary reflects a full year of service in 2021 as opposed to Ms. Mazumdar-Shaw's more limited tenure in 2020.
4 Does not include employees of Founded Entities.

Relative importance of spend on pay (unaudited)

The following table sets out the percentage change in overall spend on pay and distributions to shareholders in 2021 compared to 2020:

	2021	2020	% change
Staff costs[1]	**$22,136,823**	$18,225,744	21%
Distributions to Shareholders	**—**	—	—

1 Excludes Founded Entities.

Details of the Remuneration Committee, advisors to the Committee and their fees

The Remuneration Committee consists of Dr. LaMattina, Ms. Mazumdar-Shaw and Dr. Kucherlapati, with Dr. LaMattina serving as the Chair of the Committee. In 2021 the Committee received independent remuneration advice from Aon plc. This independent advisor was appointed by and was accountable to the Committee and provided no other services to the Company. The terms of engagement between the Committee and Aon are available from the Company Secretary on request. The Remuneration Committee also received advice from Korn Ferry (UK) Limited, who was appointed by and is accountable to the Committee but also provides certain other candidate placement services to the Company. The terms of engagement between the Committee and Korn Ferry are available from the Company Secretary on request. The Committee also consults with the Chief Executive Officer and President, and historically consulted with Mr. Muniz when he was an Executive Director and our Chief Operating Officer. However, no Director is permitted to participate in discussions or decisions about their personal remuneration. During the year, fees in respect of remuneration advice from Aon amounted to $28,490 and from Korn Ferry £32,665. Each of Aon and Korn Ferry is a founder member of the Remuneration Consultants' Group and complies with its Code of Conduct which sets out guidelines to ensure that its advice is independent and free of undue influence.

Statement of voting at general meeting (unaudited)

The table below sets out the proxy results of the vote on our Remuneration Report at our 2021 AGM:

Resolutions	For	%	Against	%	Withheld	Total votes cast
To approve the Directors' Remuneration Report	200,319,991	89.74%	22,895,826	10.26%	2,309,748	223,215,817

The table below sets out the proxy results of the vote on our Remuneration Policy at our 2020 AGM:

Resolutions	For	%	Against	%	Withheld	Total votes cast
To approve the Directors' Remuneration Policy	187,285,809	83.90%	35,930,008	16.10%	2,309,748	223,215,817

2022 AGM

The Company's AGM will be held at 11:00 am EDT (4:00 pm BST) on June 15, 2022 at the Company's headquarters at 6 Tide Street, Boston, Massachusetts. Information regarding the voting outcome will be disclosed in next year's Annual Report on Remuneration.

This report has been prepared by the Remuneration Committee and has been approved by the Board. It complies with the CA 2006 and related regulations. This report will be put to shareholders for approval at the forthcoming AGM.

On behalf of the Board of Directors

Bharatt Chowrira
Company Secretary

April 25, 2022

Independent auditor's report to the members of PureTech Health plc

1 Our opinion is unmodified

We have audited the financial statements of PureTech Health plc ("the Company") for the year ended 31 December 2021 which comprise the Consolidated statements of comprehensive Income/(Loss), Consolidated Statements of Financial Position, Consolidated Statements of Changes in Equity, Consolidated Statements of Cash Flows, Company Statement of Financial Position, Company statements of changes in Equity, Company statement of Cash Flows and the related notes, including the accounting policies in note 1.

In our opinion:

- the financial statements give a true and fair view of the state of the Group's and of the parent Company's affairs as at 31 December 2021 and of the Group's loss for the year then ended;
- the Group financial statements have been properly prepared in accordance UK-adopted international accounting standards;
- the parent Company financial statements have been properly prepared in accordance with UK-adopted international accounting standards; and
- the financial statements have been prepared in accordance with the requirements of the Companies Act 2006.

Basis for opinion

We conducted our audit in accordance with International Standards on Auditing (UK) ("ISAs (UK)") and applicable law. Our responsibilities are described below. We believe that the audit evidence we have obtained is a sufficient and appropriate basis for our opinion. Our audit opinion is consistent with our report to the audit committee.

We were first appointed as auditor by the directors on 7 September 2015. The period of total uninterrupted engagement is for the seven financial years ended 31 December 2021. We have fulfilled our ethical responsibilities under, and we remain independent of the Group in accordance with, UK ethical requirements including the FRC Ethical Standard as applied to listed public interest entities. No non-audit services prohibited by that standard were provided.

Overview

Materiality: Group group financial statements as a whole	$4.00m (2020: $1.10m) 0.4% of total assets (2020: 0.8% of total operating expenses)
Coverage	100% (2019: 100%) of total revenue, profit before tax and total assets

Key audit matters		vs 2020
Recurring risks	Valuation of financial instruments; investments in Gelesis and Akili preferred share financial assets, Vedanta and Follica preferred shares financial liabilities and Follica and Vedanta warrants financial liabilities*	◀▶
	Classification of new preferred shares and convertible loan notes including identification and classification of any embedded derivatives	◀▶
	Valuation of investments and intercompany receivable balances held by the Parent Company	◀▶

* In 2020, a Key Audit Matter relating to the valuation of financial assets was presented separately from the Key Audit Matter on the valuation of financial liabilities. In 2021, both Key Audit Matters are presented as one given the risks and our response are the same for both.

2 Key audit matters: our assessment of risks of material misstatement

Key audit matters are those matters that, in our professional judgement, were of most significance in the audit of the financial statements and include the most significant assessed risks of material misstatement (whether or not due to fraud) identified by us, including those which had the greatest effect on: the overall audit strategy; the allocation of resources in the audit; and directing the efforts of the engagement team. We summarise below the key audit matters, in decreasing order of audit significance, in arriving at our audit opinion above, together with our key audit procedures to address those matters and, as required for public interest entities, our results from those procedures. These matters were addressed, and our results are based on procedures undertaken, in the context of, and solely for the purpose of, our audit of the financial statements as a whole, and in forming our opinion thereon, and consequently are incidental to that opinion, and we do not provide a separate opinion on these matters.

	The risk	Our response
Valuation of financial instruments; investments in Gelesis and Akili preferred share financial assets, Vedanta and Follica preferred shares financial liabilities and Follica and Vedanta warrants financial liabilities The financial assets and liabilities noted above is a portion of the amounts disclosed below. **($397.2 million investments and $180.8 million preferred shares and warrant liabilities;** 2020: $530.2 million investments and $127.2m preferred shares and warrant liabilities). Refer to page 128 (Audit Committee Report), page 160 (accounting policy) and page 193 (financial disclosures).	Subjective valuation and Forecast-based valuation: The Group finances its operations partly through preferred shares, convertible notes or warrants which are classified as level 3 financial instruments and carried at fair value. The Group also holds investments in subsidiaries through preferred shares, which are classified as level 3 financial instruments and carried at fair value. Determining the fair value of these financial instruments involves a significant level of estimation due to the assumptions used, and internal and external factors that may impact the assumptions. The fair value of these financial instruments can be estimated by using a market approach, income approach or a cost / asset approach. Where the valuation is driven by an income approach there is inherent uncertainty involved in forecasting the trading of such companies in arriving at the enterprise value and the assumptions that underpin the enterprise value. The key assumptions include the discount rate, and the probability of success which mean that the valuations are sensitive to changes in these assumptions. There is significant estimation in determining the enterprise value when a market approach is taken and inputs such as term to exit and probability of exit scenarios. Where a recent transaction or agreement has been used as part of the market approach there is judgement as to the relevance of the transaction based on the specific circumstances of that investment. The effect of these matters is that, as part of our risk assessment, we determined that the valuation of financial assets and liabilities has a high degree of estimation uncertainty.	We performed the detailed tests below rather than seeking to rely on any of the group's controls because our knowledge of the design of these controls (see Audit Committee Report page 129 for further details) indicated that we would not be able to obtain the required evidence to support reliance on controls. Our procedures included: *Our valuation expertise:* Our valuation specialists critically assessed the enterprise value where derived from a market approach in an IPO scenario by comparing changes in the enterprise value to changes in the market value of comparable listed companies. Our valuation specialists evaluated the appropriateness of the discount rates when an income approach is used, by comparing the key inputs of the discount rates to publicly available market data information and assessing business changes in the company in the current year. *Our scientific expertise* Our medical specialist challenged management's assessment on the overall scientific validation and progress of each relevant fair value estimate. Assessing valuer's credentials: We used our valuation specialists to assist us in assessing the expertise and credentials of the group's external valuation specialists used in the corroboration of management's valuation. Benchmarking assumptions: Internal data such as strategic plans and external data such as public announcements are utilised for inputs such as exit dates, exit scenarios and probability of exit scenarios. Procedures performed included, inspecting strategic plans and public announcements and comparing against previous year assumptions and assessing if any changes were reasonable in the context of recent developments at the Company.

2 Key audit matters: our assessment of risks of material misstatement — continued

	The risk	Our response
		Where instruments were valued using the price of a recent transaction or agreement as an appropriate basis for the measurement of fair value we inspected agreements or correspondence to corroborate the price and we evaluated whether the transaction or event was on an arm's length by assessing whether the third party investors were independent from the Company. Where an income approach was used to derive the valuation, we evaluated the reasonableness of the probability of success used by comparing them to publicly available industry data. *Assessing transparency:* We assessed the appropriateness, in accordance with relevant accounting standards, of the disclosures related to estimation uncertainty. *Our results* We found the valuation of level 3 financial instruments to be acceptable. (2020: acceptable).
Classification of new preferred shares and convertible loan notes including identification and classification of any embedded derivatives **($63.4 million preferred shares and $2.2m convertible notes;** 2020: $25.0m convertible notes) Refer to page 128 (Audit Committee Report), page 160 (accounting policy) and page 191 and 198 (financial disclosures).	Accounting treatment The Group finances its operations partly through financial instruments and in the current period entered into a convertible loan note transaction and Vedanta issued preferred shares. There is a significant level of judgement in relation to assessing the terms of the instruments to identify whether the instruments meet the criterion to be classified as debt or equity in the issuer. There is also judgement in assessing the terms of the contracts to determine if any host instrument incudes any separable embedded derivatives and whether any separable embedded derivatives should be classified as det or equity . Due to these factors, for new convertible notes and preferred shares issued by subsidiaries in the year, this has been determined to be a significant risk.	We performed the tests below rather than seeking to rely on any of the Group's controls because the nature of the balance is such that we would expect to obtain audit evidence primarily through the detailed procedures described. Our procedures included: *Accounting analysis:* We inspected the terms of the agreements and features of the instruments and assessed these against the requirements of the accounting standards to identify whether the financial instruments should be classified as liability or equity; whether the financial instruments contained embedded derivatives; and whether any embedded derivatives should be classified as equity or liability. Assessing transparency: We have considered the adequacy of the disclosure of the accounting treatment in the financial statements and disclosure of key judgements; *Our results* We found the classification of preferred shares and convertible notes and the identification and classification of any embedded derivative within financial instruments to be acceptable. (2020: acceptable).

2 Key audit matters: our assessment of risks of material misstatement — continued

	The risk	Our response
Valuation of investments and intercompany receivable balances held by the Parent Company (**$446.0 million;** 2020: $458.6m) Refer to page 128 (Audit Committee Report), page 214 (accounting policy) and page 214 (financial disclosures).	Low risk, high value The carrying amount of the parent Company's investments in and intercompany receivables from the subsidiary companies represents 100% (2020: 100%) of the Company's total assets. The recoverability of these balances is not considered to contain a high risk of significant misstatement or be subject to significant judgement. However, due to their materiality in the context of the parent Company financial statements, this is considered to be the area which was the key focus of our overall parent Company audit.	We performed the tests below rather than seeking to rely on any of the Group's controls because the nature of the balance is such that we would expect to obtain audit evidence primarily through the detailed procedures described. Our procedures included: *Comparing valuations:* We compared the carrying amount of the investment and the intercompany receivables to the market capitalisation of the Group, as PureTech Health LLC contains all of the Group's trading operations. We compared the carrying amount of the investment and the intercompany receivables to the fair value of all the financial instruments and investments held by the group to assess for indicators of impairment. *Our results* We found the recoverability of the investments and intercompany receivable balances held by the Parent Company to be acceptable. (2020: acceptable).

3 Our application of materiality and an overview of the scope of our audit

Materiality for the group financial statements as a whole was set at $4.0m (2020:$1.1m), determined with reference to a benchmark of total assets (2020: total operating expenses), of which it represents 0.4% (2020: 0.8% of total operating expenses). The benchmark changed to total assets from total operating expenses as we assessed the users of the financial statements would be more focussed on total assets as a number of founded entities move into the next phase of their life cycle with IPOs taking place or being planned. This has resulted in realisation of the Group's investments and cash proceeds. Materiality for the parent company financial statements as a whole was set at $2.5m (2020: $0.39m), determined with reference to a benchmark of total assets, of which it represents 0.6% (2020: 0.11%).The increase in materiality in the parent company is due to the materiality being capped in prior year by component materiality of the Group.

In line with our audit methodology, our procedures on individual account balances and disclosures were performed to a lower threshold, performance materiality, so as to reduce to an acceptable level the risk that individually immaterial misstatements in individual account balances add up to a material amount across the financial statements as a whole.

Performance materiality was set at 65% (2020: 75%) of materiality for the financial statements as a whole, which equates to $2.6m (2020: $0.86m) for the group and $1.62m (2020: $0.39m) for the parent company. We applied this percentage in our determination of performance materiality based on the level of identified misstatements and control deficiencies during the prior period.

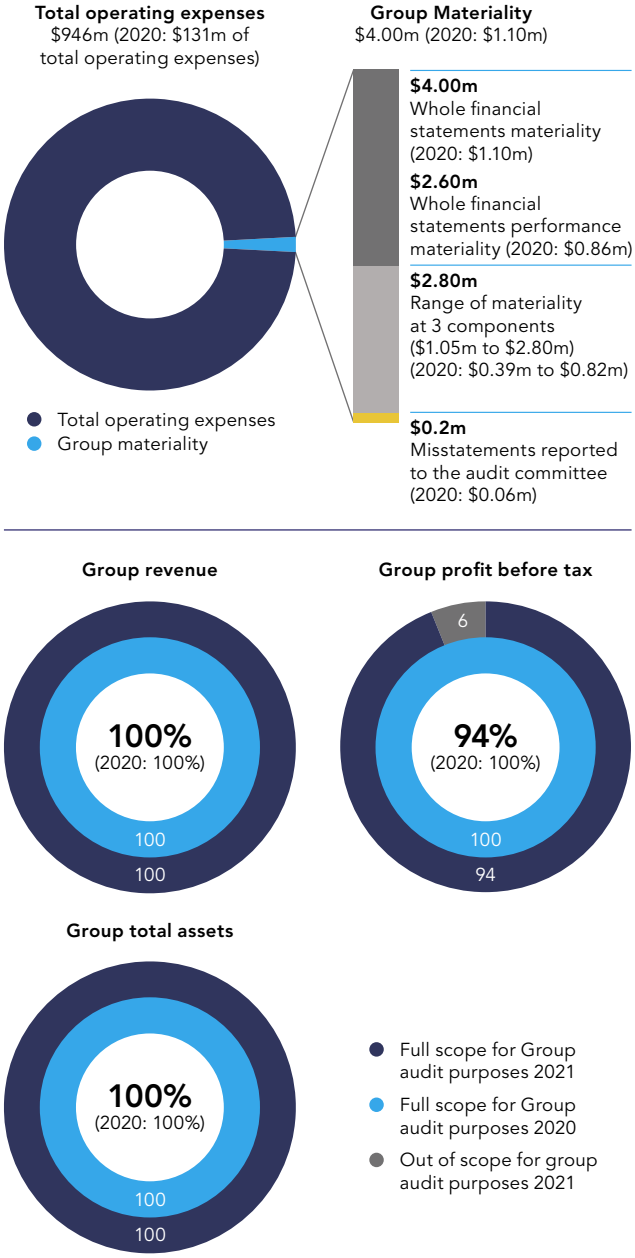
We agreed to report to the Audit Committee any corrected or uncorrected identified misstatements exceeding $0.2m, in addition to other identified misstatements that warranted reporting on qualitative grounds.

The scope of the audit work performed was fully substantive as we did not rely upon the Group's internal control over financial reporting

Of the group's 4 (2020: 4) reporting components, we subjected 3 (2020: 4) to full scope audits for group purposes. For the residual component, we performed analysis at an aggregated Group level to re-examine our assessment that there were no significant risks of material misstatement with these.

The Group team instructed component auditors as to the significant areas to be covered, including the relevant risks detailed above and the information to be reported back. The component materialities ranged from $1.05m to $2.8m, having regard to the mix of size and risk profile of the Group across the components. The work on 2 of the 3 components (2020: 2 of the 4 components) was performed by component auditors and the rest, including the audit of the parent company, was performed by the Group team.

Meetings and telephone conferences were also held with the component auditor to assess audit risk and strategy. At these meetings, the findings reported to the Group team were discussed in more detail, and any further work required by the Group team was then performed by the component auditor.



4. Going concern

The Directors have prepared the financial statements on the going concern basis as they do not intend to liquidate the Group or the Company or to cease their operations, and as they have concluded that the Group's and the Company's financial position means that this is realistic. They have also concluded that there are no material uncertainties that could have cast significant doubt over their ability to continue as a going concern for at least a year from the date of approval of the financial statements ("the going concern period").

We used our knowledge of the Group, its industry, and the general economic environment to identify the inherent risks to its business model and analysed how those risks might affect the Group's and Company's financial resources or ability to continue operations over the going concern period. The risks that we considered most likely to adversely affect the Group's and Company's available financial resources over this period were:

- Failure to raise future funding to finance the Group's strategic business model.

We considered whether these risks could plausibly affect the liquidity in the going concern period by comparing severe, but plausible downside scenarios that could arise from these risks individually and collectively against the level of available financial resources indicated by the Group's financial forecasts.

Our procedures also included:

- Critically assessing assumptions in alternative funding scenarios and overlaying knowledge of the entity' plans based on approved budgets and our knowledge of the entity and the sector in which it operates.
- We also compared past budgets to actual results to assess the directors' track record of budgeting accurately.
- We evaluated the achievability of the actions the directors consider they would take to improve the position should the risk of being unable to obtain future funding materialise, which included liquidating balance sheet assets and stopping additional investments in subsidiaries, taking into account the extent to which the directors can control the timing and outcome of these.
- We considered whether the going concern disclosure in note 1 to the financial statements gives a full and accurate description of the Directors' assessment of going concern.

Our conclusions based on this work:

- we consider that the directors' use of the going concern basis of accounting in the preparation of the financial statements is appropriate;
- we have not identified, and concur with the directors' assessment that there is not, a material uncertainty related to events or conditions that, individually or collectively, may cast significant doubt on the Group's or Company's ability to continue as a going concern for the going concern period;
- we have nothing material to add or draw attention to in relation to the directors' statement in note 1 to the financial statements on the use of the going concern basis of accounting with no material uncertainties that may cast significant doubt over the Group and Company's use of that basis for the going concern period, and we found the going concern disclosure in note 1 to be acceptable; and
- the related statement under the Listing Rules set out on page 94 is materially consistent with the financial statements and our audit knowledge.

However, as we cannot predict all future events or conditions and as subsequent events may result in outcomes that are inconsistent with judgements that were reasonable at the time they were made, the above conclusions are not a guarantee that the Group or the Company will continue in operation.

5 Fraud and breaches of laws and regulations – ability to detect

Identifying and responding to risks of material misstatement due to fraud

To identify risks of material misstatement due to fraud ("fraud risks") we assessed events or conditions that could indicate an incentive or pressure to commit fraud or provide an opportunity to commit fraud. Our risk assessment procedures included:

- Enquiring of directors, the audit committee and inspection of policy documentation as to the Group's high-level policies and procedures to prevent and detect fraud, including the Group's channel for "whistleblowing", as well as whether they have knowledge of any actual, suspected or alleged fraud.
- Reading Board, audit, remuneration and nomination committee minutes.
- Considering remuneration incentive schemes and performance targets for management and directors We communicated identified fraud risks throughout the audit team and remained alert to any indications of fraud throughout the audit. This included communication from the group to component audit teams of relevant fraud risks identified at the Group level and request to component audit teams to report to the Group audit team any instances of fraud that could give rise to a material misstatement at group.

5 Fraud and breaches of laws and regulations – ability to detect — continued

As required by auditing standards, and taking into account possible pressures to meet investor expectations and weaknesses in internal controls, we perform procedures to address the risk of management override of controls, in particular the risk that Group and component management may be in a position to make inappropriate accounting entries and the risk of bias in accounting estimates and judgements such as the valuation of financial instruments. On this audit we do not believe there is a fraud risk related to revenue recognition because management have little incentive to increase revenue on the basis that their remuneration is not dependent on it and revenue would not demonstrate progress of the business.

We also identified a fraud risk related to the valuation of financial instruments; Gelesis and Akili preferred shares financial assets, Vedanta and Follica preferred shares financial liabilities and Follica and Vedanta warrants financial liabilities in response to possible pressures to meet investor expectations and the level of estimation and judgement required.

Further detail in respect of the valuation of financial instruments is set out in the key audit matter disclosures in section 2 of this report.

We performed procedures including:

- Performing a walkthrough of the design and implementation of journals controls.
- Identifying journal entries to test for all full scope components based on risk criteria and comparing the identified entries to supporting documentation. These included those with unusual descriptions, those posted and approved by the same user, those posted to unusual accounts in relation to cash and revenue, and material post close entries.
- • Assessing whether the judgements made in making accounting estimates are indicative of a potential bias.

Identifying and responding to risks of material misstatement due to non-compliance with laws and regulations

We identified areas of laws and regulations that could reasonably be expected to have a material effect on the financial statements from our general commercial and sector experience and through discussion with the directors (as required by auditing standards) and discussed with the directors the policies and procedures regarding compliance with laws and regulations.

As the Group is regulated, our assessment of risks involved gaining an understanding of the control environment including the entity's procedures for complying with regulatory requirements.

We communicated identified laws and regulations throughout our team and remained alert to any indications of non-compliance throughout the audit. This included communication from the group to component audit teams of relevant laws and regulations identified at the Group level, and a request for component auditors to report to the group team any instances of non-compliance with laws and regulations that could give rise to a material misstatement at a group level.

The potential effect of these laws and regulations on the financial statements varies considerably.

Firstly, the Group is subject to laws and regulations that directly affect the financial statements including financial reporting legislation (including related companies legislation), distributable profits legislation and taxation legislation and we assessed the extent of compliance with these laws and regulations as part of our procedures on the related financial statement items.

Secondly, the Group is subject to many other laws and regulations where the consequences of non-compliance could have a material effect on amounts or disclosures in the financial statements, for instance through the imposition of fines or litigation. We identified the following areas as those most likely to have such an effect: health and safety, anti-bribery, employment law (including within the United States), Food and Drug Administration and European Medicines Agency regulations, 1940s Investment Act and the Securities Exchange Commission regulations. Auditing standards limit the required audit procedures to identify non-compliance with these laws and regulations to enquiry of the directors and inspection of regulatory and legal correspondence, if any. Therefore, if a breach of operational regulations is not disclosed to us or evident from relevant correspondence, an audit will not detect that breach.

Context of the ability of the audit to detect fraud or breaches of law or regulation

Owing to the inherent limitations of an audit, there is an unavoidable risk that we may not have detected some material misstatements in the financial statements, even though we have properly planned and performed our audit in accordance with auditing standards. For example, the further removed non-compliance with laws and regulations is from the events and transactions reflected in the financial statements, the less likely the inherently limited procedures required by auditing standards would identify it.

In addition, as with any audit, there remained a higher risk of non-detection of fraud, as these may involve collusion, forgery, intentional omissions, misrepresentations, or the override of internal controls. Our audit procedures are designed to detect material misstatement. We are not responsible for preventing non-compliance or fraud and cannot be expected to detect non-compliance with all laws and regulations.

6 We have nothing to report on the other information in the Annual Report and accounts

The directors are responsible for the other information presented in the Annual Report together with the financial statements. Our opinion on the financial statements does not cover the other information and, accordingly, we do not express an audit opinion or, except as explicitly stated below, any form of assurance conclusion thereon.

Our responsibility is to read the other information and, in doing so, consider whether, based on our financial statements audit work, the information therein is materially misstated or inconsistent with the financial statements or our audit knowledge. Based solely on that work we have not identified material misstatements in the other information.

Strategic report and directors' report

Based solely on our work on the other information:

- we have not identified material misstatements in the strategic report and the directors' report;
- in our opinion the information given in those reports for the financial year is consistent with the financial statements; and
- in our opinion those reports have been prepared in accordance with the Companies Act 2006.

Directors' remuneration report

In our opinion the part of the Directors' Remuneration Report to be audited has been properly prepared in accordance with the Companies Act 2006.

Disclosures of emerging and principal risks and longer-term viability

We are required to perform procedures to identify whether there is a material inconsistency between the directors' disclosures in respect of emerging and principal risks and the viability statement, and the financial statements and our audit knowledge.

Based on those procedures, we have nothing material to add or draw attention to in relation to:

- the directors' confirmation within the Viability Statement page 94 that they have carried out a robust assessment of the emerging and principal risks facing the Group, including those that would threaten its business model, future performance, solvency and liquidity;
- the Principal Risks disclosures describing these risks and how emerging risks are identified, and explaining how they are being managed and mitigated; and
- the directors' explanation in the Viability Statement of how they have assessed the prospects of the Group, over what period they have done so and why they considered that period to be appropriate, and their statement as to whether they have a reasonable expectation that the Group will be able to continue in operation and meet its liabilities as they fall due over the period of their assessment, including any related disclosures drawing attention to any necessary qualifications or assumptions.

We are also required to review the Viability Statement, set out on page 94 under the Listing Rules. Based on the above procedures, we have concluded that the above disclosures are materially consistent with the financial statements and our audit knowledge.

Our work is limited to assessing these matters in the context of only the knowledge acquired during our financial statements audit. As we cannot predict all future events or conditions and as subsequent events may result in outcomes that are inconsistent with judgements that were reasonable at the time they were made, the absence of anything to report on these statements is not a guarantee as to the Group's and Company's longer-term viability.

Corporate governance disclosures

We are required to perform procedures to identify whether there is a material inconsistency between the directors' corporate governance disclosures and the financial statements and our audit knowledge.

Based on those procedures, we have concluded that each of the following is materially consistent with the financial statements and our audit knowledge:

- the directors' statement that they consider that the annual report and financial statements taken as a whole is fair, balanced and understandable, and provides the information necessary for shareholders to assess the Group's position and performance, business model and strategy;
- the section of the annual report describing the work of the Audit Committee, including the significant issues that the audit committee considered in relation to the financial statements, and how these issues were addressed; and
- the section of the annual report that describes the review of the effectiveness of the Group's risk management and internal control systems.

We are required to review the part of Corporate Governance Statement relating to the Group's compliance with the provisions of the UK Corporate Governance Code specified by the Listing Rules for our review. We have nothing to report in this respect.

The impact of climate change on our audit

In planning our audit we performed a risk assessment to consider the potential impacts of climate change on the Group's business and its financial statements and our audit. This included making enquiries of management to understand the extent of the potential impact of climate change risk on the Group's financial statements. Taking into account the industries the Group invests in, there was no significant impact on our key audit matters

We have also read the Group's and the Parent Company's disclosure of climate related information in the front half of the annual report as set out on pages 87 to 89 and considered consistency with the financial statements and our audit knowledge.

7 We have nothing to report on the other matters on which we are required to report by exception

Under the Companies Act 2006, we are required to report to you if, in our opinion:

- adequate accounting records have not been kept by the parent Company, or returns adequate for our audit have not been received from branches not visited by us; or
- the parent Company financial statements and the part of the Directors' Remuneration Report to be audited are not in agreement with the accounting records and returns; or
- certain disclosures of directors' remuneration specified by law are not made; or
- we have not received all the information and explanations we require for our audit.

We have nothing to report in these respects.

8 Respective responsibilities

Directors' responsibilities

As explained more fully in their statement set out on page 126, the directors are responsible for: the preparation of the financial statements including being satisfied that they give a true and fair view; such internal control as they determine is necessary to enable the preparation of financial statements that are free from material misstatement, whether due to fraud or error; assessing the Group and parent Company's ability to continue as a going concern, disclosing, as applicable, matters related to going concern; and using the going concern basis of accounting unless they either intend to liquidate the Group or the parent Company or to cease operations, or have no realistic alternative but to do so.

Auditor's responsibilities

Our objectives are to obtain reasonable assurance about whether the financial statements as a whole are free from material misstatement, whether due to fraud or error, and to issue our opinion in an auditor's report. Reasonable assurance is a high level of assurance, but does not guarantee that an audit conducted in accordance with ISAs (UK) will always detect a material misstatement when it exists. Misstatements can arise from fraud or error and are considered material if, individually or in aggregate, they could reasonably be expected to influence the economic decisions of users taken on the basis of the financial statements.

A fuller description of our responsibilities is provided on the FRC's website at www.frc.org.uk/auditorsresponsibilities.

9 The purpose of our audit work and to whom we owe our responsibilities

This report is made solely to the Company's members, as a body, in accordance with Chapter 3 of Part 16 of the Companies Act 2006 and the terms of our engagement by the Company. Our audit work has been undertaken so that we might state to the Company's members those matters we are required to state to them in an auditor's report and the further matters we are required to state to them in accordance with the terms agreed with the Company, and for no other purpose. To the fullest extent permitted by law, we do not accept or assume responsibility to anyone other than the Company and the Company's members, as a body, for our audit work, for this report, or for the opinions we have formed.

Robert Seale (Senior Statutory Auditor)
for and on behalf of KPMG LLP, Statutory Auditor

Chartered Accountants
5 Canada Square
Canary Wharf
London
E14 5GL

25 April 2022

Consolidated Statements of Comprehensive Income/(Loss)

For the years ended December 31

	Note	**2021 $000s**	2020 $000s	2019 $000s
Contract revenue	3	**9,979**	8,341	8,688
Grant revenue	3	**7,409**	3,427	1,119
Total revenue		**17,388**	11,768	9,807
Operating expenses:				
General and administrative expenses	7	**(57,199)**	(49,440)	(59,358)
Research and development expenses	7	**(110,471)**	(81,859)	(85,848)
Operating income/(loss)		**(150,282)**	(119,531)	(135,399)
Other income/(expense):				
Gain on deconsolidation	5	**—**	—	264,409
Gain/(loss) on investments held at fair value	5	**179,316**	232,674	(37,863)
Loss realized on sale of investments	5	**(20,925)**	(54,976)	—
Gain on loss of significant influence	6	**—**	—	445,582
Other income/(expense)	6, 21	**1,592**	1,035	39
Other income/(expense)		**159,983**	178,732	672,167
Finance income/(costs):				
Finance income	9	**214**	1,183	4,362
Finance costs – contractual	9	**(4,771)**	(2,946)	(2,576)
Finance income/(costs) – fair value accounting	9	**9,606**	(4,351)	(46,475)
Finance income/(costs) – subsidiary preferred shares	9	**—**	—	(1,458)
Net finance income/(costs)		**5,050**	(6,115)	(46,147)
Share of net income/(loss) of associates accounted for using the equity method	6	**(73,703)**	(34,117)	30,791
Impairment of investment in associate	6	**—**	—	(42,938)
Income/(loss) before taxes		**(58,953)**	18,969	478,474
Taxation	25	**(3,756)**	(14,401)	(112,409)
Income/(Loss) for the year		**(62,709)**	4,568	366,065
Other comprehensive income/(loss):				
Items that are or may be reclassified as profit or loss				
Foreign currency translation differences		**—**	469	(10)
Total other comprehensive income/(loss)		**—**	469	(10)
Total comprehensive income/(loss) for the year		**(62,709)**	5,037	366,055
Income/(loss) attributable to:				
Owners of the Company		**(60,558)**	5,985	421,144
Non-controlling interests	18	**(2,151)**	(1,417)	(55,079)
		(62,709)	4,568	366,065
Comprehensive income/(loss) attributable to:				
Owners of the Company		**(60,558)**	6,454	421,134
Non-controlling interests	18	**(2,151)**	(1,417)	(55,079)
		(62,709)	5,037	366,055
		$	$	$
Earnings/(loss) per share:				
Basic earnings/(loss) per share	10	**(0.21)**	0.02	1.49
Diluted earnings/(loss) per share	10	**(0.21)**	0.02	1.44

The accompanying notes are an integral part of these financial statements.

Consolidated Statements of Financial Position

As of December 31,

	Note	2021 $000s	2020 $000s
Assets			
Non-current assets			
Property and equipment, net	11	**26,771**	22,777
Right of use asset, net	21	**17,166**	20,098
Intangible assets, net	12	**987**	899
Investments held at fair value	5, 16	**397,179**	530,161
Investments in associates	6	**—**	—
Lease receivable – long-term	21	**1,285**	1,700
Other non-current assets		**810**	11
Total non-current assets		**444,197**	575,645
Current assets			
Trade and other receivables	22	**3,174**	2,558
Income tax receivable	25	**4,514**	—
Prepaid expenses		**10,755**	5,405
Lease receivable – short-term	21	**415**	381
Other financial assets	13, 22	**2,124**	2,124
Short-term note from associate	16	**15,120**	—
Cash and cash equivalents	22	**465,708**	403,881
Total current assets		**501,809**	414,348
Total assets		**946,006**	989,994
Equity and liabilities			
Equity			
Share capital	14	**5,444**	5,417
Share premium	14	**289,303**	288,978
Merger reserve	14	**138,506**	138,506
Translation reserve	14	**469**	469
Other reserve	14	**(40,077)**	(24,050)
Retained earnings/(accumulated deficit)	14	**199,871**	260,429
Equity attributable to the owners of the Company		**593,515**	669,748
Non-controlling interests	14, 18	**(9,368)**	(16,209)
Total equity		**584,147**	653,539
Non-current liabilities			
Deferred tax liability	25	**89,765**	108,626
Lease liability, non-current	21	**29,040**	32,088
Long-term loan	20	**14,261**	14,818
Liability for share based awards	8	**2,659**	—
Total non-current liabilities		**135,725**	155,531
Current liabilities			
Deferred revenue	3	**65**	1,472
Lease liability, current	21	**3,950**	3,261
Trade and other payables	19	**35,817**	21,826
Subsidiary:			
Notes payable	16, 17	**3,916**	26,455
Warrant liability	16	**6,787**	8,206
Preferred shares	15, 16	**174,017**	118,972
Current portion of long-term loan	20	**857**	—
Other current liabilities		**726**	732
Total current liabilities		**226,135**	180,924
Total liabilities		**361,859**	336,455
Total equity and liabilities		**946,006**	989,994

Please refer to the accompanying Notes to the consolidated financial information. Registered number: 09582467.
The Consolidated Financial Statements were approved by the Board of Directors and authorized for issuance on April 25, 2022 and signed on its behalf by:

Daphne Zohar
Chief Executive Officer
April 25, 2022

The accompanying notes are an integral part of these financial statements.

Consolidated Statements of Changes in Equity

For the years ended December 31

	Share Capital									
	Shares	Amount $000s	Share premium $000s	Merger reserve $000s	Translation reserve $000s	Other reserve $000s	Retained earnings/ (accumulated deficit) $000s	Total Parent equity $000s	Non-controlling interests $000s	Total Equity $000s
Balance January 1, 2019	282,493,867	5,375	278,385	138,506	10	20,923	(166,693)	276,506	(108,535)	167,971
Net income/(loss)	—	—	—	—	—	—	421,144	421,144	(55,079)	366,065
Foreign currency exchange	—	—	—	—	(10)	—	—	(10)	—	(10)
Total comprehensive income/(loss) for the year	**—**	**—**	**—**	**—**	**(10)**	**—**	**421,144**	**421,134**	**(55,079)**	**366,055**
Deconsolidation of subsidiary	—	—	—	—	—	—	—	—	97,178	97,178
Subsidiary note conversion and changes in NCI ownership interest	—	—	—	—	—	(20,631)	—	(20,631)	23,049	2,418
Exercise of share-based awards	237,090	5	499	—	—	—	—	504	—	504
Purchase of subsidiary's non-controlling interest through issuance of shares	2,126,338	28	9,078	—	—	(33,145)	—	(24,039)	24,039	—
Revaluation of deferred tax assets related to share-based awards	—	—	—	—	—	3,061	—	3,061	—	3,061
Equity settled share-based payments	—	—	—	—	—	12,785	—	12,785	1,683	14,468
Vesting of restricted stock units (RSU)	513,324	—	—	—	—	(1,280)	—	(1,280)	—	(1,280)
Other	—	—	—	—	—	5	(7)	(2)	25	23
Balance December 31, 2019	**285,370,619**	**5,408**	**287,962**	**138,506**	**—**	**(18,282)**	**254,444**	**668,037**	**(17,639)**	**650,398**
Net income/(loss)	—	—	—	—	—	—	5,985	5,985	(1,417)	4,568
Foreign currency exchange	—	—	—	—	469	—	—	469	—	469
Total comprehensive income/(loss) for the year	**—**	**—**	**—**	**—**	**469**	**—**	**5,985**	**6,454**	**(1,417)**	**5,037**
Exercise of share-based awards	514,406	9	1,016	—	—	—	—	1,025	11	1,036
Revaluation of deferred tax assets related to share-based awards	—	—	—	—	—	(684)	—	(684)	—	(684)
Equity settled share-based awards	—	—	—	—	—	7,805	—	7,805	2,822	10,627
Settlement of restricted stock units	—	—	—	—	—	(12,888)	—	(12,888)	—	(12,888)
Other	—	—	—	—	—	—	—	—	13	13
As at December 31, 2020	**285,885,025**	**5,417**	**288,978**	**138,506**	**469**	**(24,050)**	**260,429**	**669,748**	**(16,209)**	**653,539**
Net income/(loss)	—	—	—	—	—	—	(60,558)	(60,558)	(2,151)	(62,709)
Foreign currency exchange	—	—	—	—	—	—	—	—	—	—
Total comprehensive income/(loss) for the year	**—**	**—**	**—**	**—**	**—**	**—**	**(60,558)**	**(60,558)**	**(2,151)**	**(62,709)**
Exercise of share-based awards	1,911,560	27	326	—	—	—	—	352	—	352
Revaluation of deferred tax assets related to share-based awards	—	—	—	—	—	615	—	615	—	615
Equity settled share-based awards	—	—	—	—	—	7,109	—	7,109	6,252	13,361
Settlement of restricted stock units	—	—	—	—	—	(10,749)	—	(10,749)	—	(10,749)
Reclassification of equity settled awards to liability awards	—	—	—	—	—	(6,773)	—	(6,773)	—	(6,773)
Vesting of share-based awards and net share exercise	—	—	—	—	—	(2,582)	—	(2,582)	—	(2,582)
Acquisition of subsidiary non-controlling interest	—	—	—	—	—	(9,636)	—	(9,636)	8,668	(968)
NCI exercise of share-based awards in subsidiaries	—	—	—	—	—	5,988	—	5,988	(5,922)	66
Distributions	—	—	—	—	—	—	—	—	(6)	(6)
Balance December 31, 2021	**287,796,585**	**5,444**	**289,303**	**138,506**	**469**	**(40,077)**	**199,871**	**593,515**	**(9,368)**	**584,147**

The accompanying notes are an integral part of these financial statements.

Consolidated Statements of Cash Flows

For the years ended December 31

	Note	2021 $000s	2020 $000s	2019 $000s
Cash flows from operating activities				
Income/(loss)		**(62,709)**	4,568	366,065
Adjustments to reconcile net operating loss to net cash used in operating activities:				
Non-cash items:				
Depreciation and amortization	11, 12	**7,287**	6,645	6,665
Impairment of investment in associate	6	**—**	—	42,938
Equity settled share-based payment expense	8	**13,950**	10,718	14,468
(Gain)/loss on investments held at fair value	5	**(179,316)**	(232,674)	37,863
Realized loss on sale of investments		**20,925**	54,976	—
Gain on deconsolidation	5	**—**	—	(264,409)
Gain on loss of significant influence	5	**—**	—	(445,582)
Loss on disposal of assets	11	**53**	66	140
Share of net (income)/loss of associates accounted for using the equity method	6	**73,703**	34,117	(30,791)
Fair value gain on derivative	6	**(800)**	—	—
Income taxes, net	25	**3,756**	14,402	112,077
Finance costs, net	9	**(5,050)**	6,114	46,229
Changes in operating assets and liabilities:				
Accounts receivable	22	**(617)**	(529)	747
Other financial assets	13	**—**	—	(48)
Prepaid expenses and other current assets		**(5,350)**	(3,371)	(25)
Deferred revenues	3	**(1,407)**	(5,223)	186
Trade and other payables	19	**8,338**	605	11,166
Other liabilities		**—**	(7)	3,002
Other		**(103)**	—	—
Income taxes paid		**(27,766)**	(20,737)	—
Interest received		**214**	1,155	3,648
Interest paid	20, 21	**(3,382)**	(2,651)	(2,495)
Net cash used in operating activities		**(158,274)**	(131,827)	(98,156)
Cash flows from investing activities:				
Purchase of property and equipment	11	**(5,571)**	(5,170)	(12,138)
Proceeds from sale of property and equipment		**30**	—	—
Purchases of intangible assets	12	**(90)**	(254)	(400)
Purchase of associate preferred shares held at fair value	5, 6	**—**	(10,000)	(13,670)
Purchase of investments held at fair value	5	**(500)**	(1,150)	(1,556)
Sale of investments held at fair value	5	**218,125**	350,586	9,294
Receipt of payment of sublease	21	**381**	350	191
Purchase of short-term note from associate	16	**(15,000)**	—	—
Purchase of convertible note	6	**—**	—	(6,480)
Cash derecognized upon loss of control over subsidiary		**—**	—	(16,036)
Purchases of short-term investments	22	**—**	—	(69,541)
Proceeds from maturity of short-term investments	22	**—**	30,116	173,995
Net cash provided by investing activities		**197,375**	364,478	63,659
Cash flows from financing activities:				
Receipt of PPP loan		**—**	68	—
Issuance of long term loan	20	**—**	14,720	—
Issuance of subsidiary preferred Shares	15	**37,610**	13,750	51,048
Proceeds from issuance of convertible notes in subsidiary	17	**2,215**	25,000	1,606
Payment of lease liability	21	**(3,375)**	(2,908)	(1,678)
Repayment of long-term debt		**—**	—	(178)
Distribution to Tal shareholders		**—**	—	(112)
Exercise of stock options		**352**	1,036	504
Settlement of RSU's		**(10,749)**	(12,888)	—
Vesting of restricted stock units and net share exercise		**(2,582)**	—	(1,280)
Issuance of shares to NCI in subsidiary	15	**66**	—	—
Issuance of warrants		**—**	92	—
Acquisition of a non-controlling Interest of a subsidiary		**(806)**	—	—
Other		**(5)**	—	—
Net cash provided by financing activities		**22,727**	38,869	49,910
Effect of exchange rates on cash and cash equivalents		**—**	—	(104)
Net increase in cash and cash equivalents		**61,827**	271,520	15,309
Cash and cash equivalents at beginning of year		**403,881**	132,360	117,051
Cash and cash equivalents at end of year		**465,708**	403,881	132,360
Supplemental disclosure of non-cash investment and financing activities:				
Purchase of non controlling interest in consideration for issuance of shares and options		**—**	—	9,106
Purchase of intangible asset and investment held at fair value in consideration for issuance of warrant liability and assumption of other long and short-term liabilities		**—**	—	15,894
Purchase of property, plant and equipment against trade and other payables	11	**1,841**	—	—
Leasehold improvements purchased through lease incentives (deducted from Right of Use Asset)	11	**1,010**	—	10,680
Conversion of subsidiary convertible note into preferred share liabilities	17	**25,797**	—	4,894
Conversion of subsidiary convertible note into subsidiary common stock (NCI)		**—**	—	2,418
Supplemental disclosure of cash paid for income taxes:				
Cash paid for income taxes		**27,766**	20,737	176

The accompanying notes are an integral part of these financial statements.

Notes to the Condensed Consolidated Financial Statements

1. Accounting policies

Description of Business

PureTech Health plc ("PureTech," the "Parent" or the "Company") is a public company incorporated, domiciled and registered in the United Kingdom ("UK"). The registered number is 09582467 and the registered address is 8th Floor, 20 Farringdon Street, London EC4A 4AB, United Kingdom.

PureTech's group financial statements consolidate those of the Company and its subsidiaries (together referred to as the "Group"). The Parent company financial statements present financial information about the Company as a separate entity and not about its Group.

The accounting policies set out below have, unless otherwise stated, been applied consistently to all periods presented in these group financial statements.

Basis of Presentation

The consolidated financial statements of the Group are presented as of December 31, 2021 and 2020, and for the years ended December 31, 2021, 2020 and 2019. The Group financial statements have been approved by the Directors on April 25, 2022, and are prepared in accordance with UK-adopted International Financial Reporting Standards (IFRSs). The Consolidated Financial Statements also comply fully with IFRSs as issued by the International Accounting Standards Board (IASB). UK-adopted IFRSs differs in certain respects from IFRS as issued by the IASB. However, the differences have no impact for the periods presented.

For presentation of the Consolidated Statements of Comprehensive Income/(Loss), the Company uses a classification based on the function of expenses, rather than based on their nature, as it is more representative of the format used for internal reporting and management purposes and is consistent with international practice.

Certain amounts in the Consolidated Financial Statements and accompanying notes may not add due to rounding. All percentages have been calculated using unrounded amounts.

Basis of Measurement

The consolidated financial statements are prepared on the historical cost basis except that the following assets and liabilities are stated at their fair value: investments held at fair value, short-term note from associate and liabilities classified as fair value through the profit or loss.

Use of Judgments and Estimates

In preparing these consolidated financial statements, management has made judgements, estimates and assumptions that affect the application of the Group's accounting policies and the reported amounts of assets, liabilities, income and expenses. Actual results may differ from these estimates. Estimates and underlying assumptions are reviewed on an on-going basis.

Significant estimation is applied in determining the following:

- Financial instruments valuations (Note 16): when estimating the fair value of subsidiary warrants, convertible notes and subsidiary preferred shares carried at fair value through profit and loss (FVTPL) as well as investments held at fair value, at initial recognition and upon subsequent measurement. This includes determining the appropriate valuation methodology and making certain estimates of the future earnings potential of the subsidiary businesses, appropriate discount rate, estimated time to exit, marketability and other industry and company specific risk factors. See Note 16 for the sensitivity analysis for key estimates used in these valuations.

Significant judgement is also applied in determining the following:

- Subsidiary preferred shares liability classification (Note 15): when determining the classification of financial instruments in terms of liability or equity. These judgements include an assessment of whether the financial instruments include any embedded derivative features, whether they include contractual obligations of the Group to deliver cash or other financial assets or to exchange financial assets or financial liabilities with another party, and whether that obligation will be settled by the Company exchanging a fixed amount of cash or other financial assets for a fixed number of its own equity instruments. Further information about these critical judgements and estimates is included below under Financial Instruments.
- When the power to control the subsidiaries exists (please refer to Notes 5 and 6 and accounting policy below Subsidiaries). This judgement includes an assessment of whether the Company has (i) power over the investee; (ii) exposure, or rights, to variable returns from its involvement with the investee; and (iii) the ability to use its power over the investee to affect the amount of the investor's returns. The Company considers among others its voting shares, shareholder agreements, ability to appoint board members, representation on the board, rights to appoint management, de facto control, investee dependence on the Company etc. If the power to control investees exists we consolidate the financial statements of such investee in the consolidated financial statements of the Group. Upon issuance of new shares in a subsidiary and a resulting change in any shareholders or governance agreements, the Group reassesses its ability to control the investee based on the revised board composition and revised subsidiary governance and management structure. When such new circumstances result in the Group losing its power to control the investee, the investee is deconsolidated.

1. Accounting policies — continued

- Whether the Company has significant influence over financial and operating policies of investees in order to determine if the Company should account for its investment as an associate based on IAS 28 or based on IFRS 9, Financial Instruments (please refer to Note 5). This judgement includes, among others, an assessment whether the Company has representation on the Board of Directors of the investee, whether the Company participates in the policy making processes of the investee, whether there is any interchange of managerial personnel, whether there is any essential technical information provided to the investee and if there are any transactions between the Company and the investee.
- Upon determining that the Company does have significant influence over the financial and operating policies of an investee, if the Company holds more than a single instrument issued by its equity-accounted investee, judgement is required to determine whether the additional instrument forms part of the investment in the associate, which is accounted for under IAS 28 and scoped out of IFRS 9, or it is a separate financial instrument that falls in the scope of IFRS 9 (please refer to Notes 5 and 6). This judgement includes an assessment of the characteristics of the financial instrument of the investee held by the Company and whether such financial instrument provides access to returns underlying an ownership interest.
- Where the company has other investments in an equity accounted investee that are not accounted for under IAS 28, judgement is required in determining if such investments constitute Long-Term Interests for the purposes of IAS 28 (please refer to Notes 5 and 6). This determination is based on the individual facts and circumstances and characteristics of each investment, but is driven, among other factors, by the intention and likelihood to settle the instrument through redemption or repayment in the foreseeable future, and whether or not the investment is likely to be converted to common stock or other equity instruments (please also refer to accounting policy with regard to Investments in Associates below). When considering the individual facts and circumstances of the Group's investment in its associate's preferred stock in the manner described above, including the long-term nature of such investment, the ability of the Group to convert its preferred stock investment to an investment in common shares and the likelihood of such conversion, as well the fact that there is no planned redemption or other settlement of the preferred stock by the investee in the foreseeable future, we concluded that such investment is considered a Long Term Interest.

As of December 31, 2021, the Group had cash and cash equivalents of $465.7 million. Considering the Group's and the Company's financial position as of December 31, 2021, and its principal risks and opportunities, a going concern analysis has been prepared for at least the twelve-month period from the date of signing the Consolidated Financial Statements ("the going concern period") utilizing realistic scenarios and applying a severe but plausible downside scenario. Even under the downside scenario, the analysis demonstrates the Group and the Company continue to maintain sufficient liquidity headroom and continue to comply with all financial obligations. The Directors believe the Group and the Company is adequately resourced to continue in operational existence for at least the twelve-month period from the date of signing the Consolidated Financial Statements, irrespective of uncertainty regarding the duration and severity of the COVID-19 pandemic and the global macroeconomic impact of the pandemic. Accordingly, the Directors considered it appropriate to adopt the going concern basis of accounting in preparing the Consolidated Financial Statements and the PureTech Health plc Financial Statements.

Basis of consolidation

The consolidated financial information as of December 31, 2021 and 2020, and for each of the years ended December 31, 2021, 2020 and 2019, comprises an aggregation of financial information of the Company and the consolidated financial information of PureTech Health LLC ("PureTech LLC"). Intra-group balances and transactions, and any unrealized income and expenses arising from intra-group transactions, are eliminated.

Subsidiaries

As used in these financial statements, the term subsidiaries refers to entities that are controlled by the Group. Financial results of subsidiaries of the Group as of December 31, 2021, are reported within the Internal segment, Controlled Founded Entities segment or the Parent Company and Other section (please refer to Note 4). Under applicable accounting rules, the Group controls an entity when it is exposed to, or has the rights to, variable returns from its involvement with the entity and has the ability to affect those returns through its power over the entity. In assessing control, the Group takes into consideration potential voting rights, board representation, shareholders' agreements, ability to appoint Directors and management, de facto control and other related factors. The financial statements of subsidiaries are included in the consolidated financial statements from the date that control commences until the date that control ceases. Losses applicable to the non-controlling interests in a subsidiary are allocated to the non-controlling interests even if doing so causes the non-controlling interests to have a deficit balance.

A list of all current and former subsidiaries organized with respect to classification as of December 31, 2021, and the Group's total voting percentage, based on outstanding voting common and preferred shares as of December 31, 2021, 2020 and 2019, is outlined below. All current subsidiaries are domiciled within the United States and conduct business activities solely within the United States.

1. Accounting policies — continued

	Voting percentage at December 31, through the holdings in					
	2021		2020		2019	
Subsidiary	**Common**	**Preferred**	Common	Preferred	Common	Preferred
Subsidiary operating companies						
Alivio Therapeutics, Inc.[1,2]	**—**	**100.0**	—	91.9	—	91.9
Entrega, Inc. (indirectly held through Enlight)[1,2]	**—**	**77.3**	—	83.1	—	83.1
Follica, Incorporated[1,2,5]	**28.7**	**56.7**	28.7	56.7	28.7	56.7
PureTech LYT (formerly Ariya Therapeutics, Inc.)	**—**	**100.0**	—	100.0	—	100.0
PureTech LYT-100	**—**	**100.0**	—	100.0	—	100.0
PureTech Management, Inc.[3]	**100.0**	**—**	100.0	—	100.0	—
PureTech Health LLC[3]	**100.0**	**—**	100.0	—	100.0	—
Sonde Health, Inc.[1,2]	**—**	**51.8**	—	51.8	—	64.1
Vedanta Biosciences, Inc.[1,2]	**—**	**48.6**	—	59.3	—	61.8
Vedanta Biosciences Securities Corp. (indirectly held through Vedanta)[1,2]	**—**	**48.6**	—	59.3	—	61.8
Deconsolidated former subsidiary operating companies						
Akili Interactive Labs, Inc.[2]	**—**	**26.7**	—	41.9	—	41.9
Gelesis, Inc.[1,2,7,10]	**4.8**	**19.7**	4.9	20.2	5.7	20.2
Karuna Therapeutics, Inc.[1,2,8]	**5.6**	**—**	12.6	—	28.4	—
Vor Biopharma Inc.[1,2,9]	**8.6**	**—**	—	16.4	—	47.5
Nontrading holding companies						
Endra Holdings, LLC (held indirectly through Enlight)[2]	**86.0**	**—**	86.0	—	86.0	—
Ensof Holdings, LLC (held indirectly through Enlight)[2]	**86.0**	**—**	86.0	—	86.0	—
PureTech Securities Corp.[2]	**100.0**	**—**	100.0	—	100.0	—
PureTech Securities II Corp.[2]	**100.0**	**—**	100.0	—	—	—
Inactive subsidiaries						
Appeering, Inc.[2]	**—**	**100.0**	—	100.0	—	100.0
Commense Inc.[2,6]	**—**	**99.1**	—	99.1	—	99.1
Enlight Biosciences, LLC[2]	**86.0**	**—**	86.0	—	86.0	—
Ensof Biosystems, Inc. (held indirectly through Enlight)[1,2]	**57.7**	**28.3**	57.7	28.3	57.7	28.3
Knode Inc. (indirectly held through Enlight)[2]	**—**	**86.0**	—	86.0	—	86.0
Libra Biosciences, Inc.[2]	**—**	**100.0**	—	100.0	—	100.0
Mandara Sciences, LLC[2]	**98.3**	**—**	98.3	—	98.3	—
Tal Medical, Inc.[1,2]	**—**	**100.0**	—	100.0	—	100.0

1 The voting percentage is impacted by preferred shares that are classified as liabilities, which results in the ownership percentage not being the same as the ownership percentage used in allocations to non-controlling interests disclosed in Note 18. The allocation of losses/profits to the noncontrolling interest is based on the holdings of subordinated stock that provide ownership rights in the subsidiaries. The ownership of liability classified preferred shares are quantified in Note 15.

2 Registered address is Corporation Trust Center, 1209 Orange St., Wilmington, DE 19801, USA.

3 Registered address is 2711 Centerville Rd., Suite 400, Wilmington, DE 19808, USA.

4 The Company's interests in its subsidiaries are predominantly in the form of preferred shares, which have a liquidation preference over the common stock, are convertible into common stock at the holder's discretion or upon certain liquidity events, are entitled to one vote per share on all matters submitted to shareholders for a vote and entitled to receive dividends when and if declared. In the case of Enlight, Mandara and PureTech Health LLC, the holdings are membership interests in an LLC. The holders of common stock are entitled to one vote per share on all matters submitted to shareholders for a vote and entitled to receive dividends when and if declared.

5 On July 19, 2019, all of the outstanding notes, plus accrued interest, issued by Follica to PureTech converted into 15,216,214 shares of Series A-3 Preferred Shares and 12,777,287 shares of common share pursuant to a Series A-3 Note Conversion Agreement between Follica and the noteholders. Please refer to Note 16.

6 Commense turned inactive during 2019.

7 On July 1, 2019 PureTech lost control of Gelesis and Gelesis was deconsolidated from the Group's financial statements, resulting in only the profits and losses generated by Gelesis through the deconsolidation date being included in the Group's Consolidated Statement of Comprehensive Income/(Loss). See Notes 5 and 6 for further details about the accounting for the investments in Gelesis subsequent to deconsolidation.

8 On March 15, 2019, PureTech lost control of Karuna, Karuna was deconsolidated from the Group's financial statements and is no longer considered a subsidiary. This results in only the profits and losses generated by Karuna through the deconsolidation date being included in the Group's Consolidated Statement of Comprehensive Income/(Loss).. See Note 5 for further details about the accounting for the investment in Karuna subsequent to deconsolidation.

9 On February 12, 2019, PureTech lost control of Vor, Vor was deconsolidated from the Group's financial statements and is no longer considered a subsidiary. This results in only the profits and losses generated by Vor through the deconsolidation date being included in the Group's Consolidated Statement of Comprehensive Income/(Loss). See Note 5 for further details about the accounting for the investment in Vor subsequent to deconsolidation.

10 See note 26 regarding Gelesis business combination with Capstar Special Purpose Acquisition Corp after balance sheet date and the Group's ownership rights in the new combined public entity.

Change in subsidiary ownership and loss of control

Changes in the Group's interest in a subsidiary that do not result in a loss of control are accounted for as equity transactions.

Where the Group loses control of a subsidiary, the assets and liabilities are derecognized along with any related non-controlling interest ("NCI"). Any interest retained in the former subsidiary is measured at fair value when control is lost. Any resulting gain or loss is recognized as profit or loss in the Consolidated Statements of Comprehensive Income/(Loss).

1. Accounting policies — continued

Associates

As used in these financial statements, the term associates are those entities in which the Group has no control but maintains significant influence over the financial and operating policies. Significant influence is presumed to exist when the Group holds between 20 and 50 percent of the voting power of an entity, unless it can be clearly demonstrated that this is not the case. The Group evaluates if it maintains significant influence over associates by assessing if the Group has lost the power to participate in the financial and operating policy decisions of the associate.

Application of the equity method to associates

Associates are accounted for using the equity method (equity accounted investees) and are initially recognized at cost, or if recognized upon deconsolidation they are initially recorded at fair value at the date of deconsolidation. The consolidated financial statements include the Group's share of the total comprehensive income and equity movements of equity accounted investees, from the date that significant influence commences until the date that significant influence ceases.

To the extent the Group holds interests in associates that are not providing access to returns underlying ownership interests, the instrument held by PureTech is accounted for in accordance with IFRS 9 as investments held at fair value.

When the Group's share of losses exceeds its equity method investment in the investee, losses are applied against Long-Term Interests, which are investments accounted for under IFRS 9. Investments are determined to be Long-Term Interests when they are long-term in nature and in substance they form part of the Group's net investment in that associate. This determination is impacted by many factors, among others, whether settlement by the investee through redemption or repayment is planned or likely in the foreseeable future, whether the investment can be converted and/or is likely to be converted to common stock or other equity instrument and other factors regarding the nature of the investment. Whilst this assessment is dependent on many specific facts and circumstances of each investment, typically conversion features whereby the investment is likely to convert to common stock or other equity instruments would point to the investment being a Long-Term Interest. Similarly, where the investment is not planned or likely to be settled through redemption or repayment in the foreseeable future, this would indicate that the investment is a Long-Term Interest. When the net investment in the associate, which includes the Group's investments in other long-term interests, is reduced to nil, recognition of further losses is discontinued except to the extent that the Group has incurred legal or constructive obligations or made payments on behalf of an investee.

The Group has also adopted the amendments to IAS 28 Investments in Associates that addresses the dual application of IAS 28 and IFRS 9 (see below) when equity method losses are applied against Long-Term Interests (LTI). The amendments provide the annual sequence in which both standards are to be applied in such a case. The Group has applied the equity method losses to the LTIs presented as part of Investments held at fair value subsequent to remeasuring such investments to their fair value at balance sheet date.

Financial Instruments

Classification

The Group classifies its financial assets in the following measurement categories:

- Those to be measured subsequently at fair value (either through other comprehensive income, or through profit or loss), and
- Those to be measured at amortized cost.

The classification depends on the Group's business model for managing the financial assets and the contractual terms of the cash flows.

For assets measured at fair value, gains and losses will are recorded in profit or loss. For investments in debt instruments, this will depend on the business model in which the investment is held. For investments in equity instruments that are not held for trading, this will depend on whether the Group has made an irrevocable election at the time of initial recognition to account for the equity investment at FVOCI. As of balance sheet dates, none of the Company's financial assets are accounted for as FVOCI.

Measurement

At initial recognition, the Group measures a financial asset at its fair value plus, in the case of a financial asset not at FVTPL, transaction costs that are directly attributable to the acquisition of the financial asset. Transaction costs of financial assets that are carried at FVTPL are expensed.

Impairment

The Group assesses on a forward-looking basis the expected credit losses associated with its debt instruments carried at amortized cost. The Group had no debt instruments carried at amortized cost as of balance sheet date. For trade receivables, the Group applies the simplified approach permitted by IFRS 9, which requires expected lifetime losses to be recognized from initial recognition of the receivables.

Financial Assets

The Group's financial assets consist of cash and cash equivalents, trade and other receivables, investments in equity securities, short-term note, other deposits and investments in associates' preferred shares. The Group's financial assets are classified into the following categories: investments held at fair value, trade and other receivables, short-term investments (if applicable) and cash and cash equivalents. The Group determines the classification of financial assets at initial recognition depending on the purpose for which the financial assets were acquired.

1. Accounting policies — continued

Investments held at fair value are investments in equity instruments that are not held for trading. Such investments consist of the Group's minority interest holdings where the Group has no significant influence or preferred share investments in the Group's associates that are not providing access to returns underlying ownership interests. These financial assets are initially measured at fair value and subsequently re-measured at fair value at each reporting date. The Company elects if the gain or loss will be recognized in Other Comprehensive Income/(Loss) or through profit and loss on an instrument by instrument basis. The Company has elected to record the changes in fair values for the financial assets falling under this category through profit and loss. Please refer to Note 5.

Changes in the fair value of financial assets at FVTPL are recognized in other income/(expense) in the Consolidated Statements of Comprehensive Income/(Loss) as applicable.

The short term note from an associate, since its contractual terms do not consist solely of cash flow payments of principal and interest on the principal amount outstanding, is initially and subsequently measured at fair value, with changes in fair value recognized through profit and loss.

Trade and other receivables are non-derivative financial assets with fixed and determinable payments that are not quoted on active markets. These financial assets are carried at the amounts expected to be received less any expected lifetime losses. Such losses are determined taking into account previous experience, credit rating and economic stability of counterparty and economic conditions. When a trade receivable is determined to be uncollectible, it is written off against the available provision. Trade and other receivables are included in current assets, unless maturities are greater than 12 months after the end of the reporting period.

Financial Liabilities

The Group's financial liabilities consist of trade and other payables, subsidiary notes payable, preferred shares, and warrant liability. Warrant liabilities are initially recognized at fair value. After initial recognition, these financial liabilities are re-measured at FVTPL using an appropriate valuation technique. Subsidiary notes payable without embedded derivatives are accounted for at amortized cost.

The majority of the Group's subsidiaries have preferred shares and notes payable with embedded derivatives, which are classified as current liabilities. When the Group has preferred shares and notes with embedded derivatives that qualify for bifurcation, the Group has elected to account for the entire instrument as FVTPL after determining under IFRS 9 that the instrument qualifies to be accounted for under such FVTPL method.

The Group derecognizes a financial liability when its contractual obligations are discharged, cancelled or expire.

Equity Instruments Issued by the Group

Financial instruments issued by the Group are treated as equity only to the extent that they meet the following two conditions, in accordance with IAS 32:

1. They include no contractual obligations upon the Group to deliver cash or other financial assets or to exchange financial assets or financial liabilities with another party under conditions that are potentially unfavorable to the Group; and
2. Where the instrument will or may be settled in the Group's own equity instruments, it is either a non-derivative that includes no obligation to deliver a variable number of the Group's own equity instruments or is a derivative that will be settled by the Group exchanging a fixed amount of cash or other financial assets for a fixed number of its own equity instruments.

To the extent that this definition is not met, the financial instrument is classified as a financial liability. Where the instrument so classified takes the legal form of the Group's own shares, the amounts presented in the Group's shareholders' equity`exclude amounts in relation to those shares.

Changes in the fair value of liabilities at FVTPL are recognized in Net finance income (costs) in the Consolidated Statements of Comprehensive Income/(Loss) as applicable.

IFRS 15, Revenue from Contracts with Customers

The standard establishes a five-step principle-based approach for revenue recognition and is based on the concept of recognizing an amount that reflects the consideration for performance obligations only when they are satisfied and the control of goods or services is transferred.

The majority of the Group's contract revenue is generated from licenses and services, some of which are part of collaboration arrangements.

Management reviewed contracts where the Group received consideration in order to determine whether or not they should be accounted for in accordance with IFRS 15. To date, PureTech has entered into transactions that generate revenue and meet the scope of either IFRS 15 or IAS 20 Accounting for Government Grants. Contract revenue is recognized at either a point-in-time or over time, depending on the nature of the performance obligations.

1. Accounting policies — continued

The Group accounts for agreements that meet the definition of IFRS 15 by applying the following five step model:

- Identify the contract(s) with a customer – A contract with a customer exists when (i) the Group enters into an enforceable contract with a customer that defines each party's rights regarding the goods or services to be transferred and identifies the payment terms related to those goods or services, (ii) the contract has commercial substance and, (iii) the Group determines that collection of substantially all consideration for goods or services that are transferred is probable based on the customer's intent and ability to pay the promised consideration.
- Identify the performance obligations in the contract – Performance obligations promised in a contract are identified based on the goods or services that will be transferred to the customer that are both capable of being distinct, whereby the customer can benefit from the good or service either on its own or together with other resources that are readily available from third parties or from the Group, and are distinct in the context of the contract, whereby the transfer of the goods or services is separately identifiable from other promises in the contract.
- Determine the transaction price – The transaction price is determined based on the consideration to which the Group will be entitled in exchange for transferring goods or services to the customer. To the extent the transaction price includes variable consideration, the Group estimates the amount of variable consideration that should be included in the transaction price utilizing either the expected value method or the most likely amount method depending on the nature of the variable consideration. Variable consideration is included in the transaction price if, in the Group's judgement, it is probable that a significant future reversal of cumulative revenue under the contract will not occur.
- Allocate the transaction price to the performance obligations in the contract – If the contract contains a single performance obligation, the entire transaction price is allocated to the single performance obligation. Contracts that contain multiple performance obligations require an allocation of the transaction price to each performance obligation based on a relative standalone selling price basis.
- Recognize revenue when (or as) the Group satisfies a performance obligation – The Group satisfies performance obligations either over time or at a point in time as discussed in further detail below. Revenue is recognized at the time the related performance obligation is satisfied by transferring a promised good or service to a customer.

Revenue generated from services agreements (typically where licenses and related services were combined into one performance obligation) is determined to be recognized over time when it can be determined that the services meet one of the following: (a) the customer simultaneously receives and consumes the benefits provided by the entity's performance as the entity performs; (b) the entity's performance creates or enhances an asset that the customer controls as the asset is created or enhanced; or (c) the entity's performance does not create an asset with an alternative use to the entity and the entity has an enforceable right to payment for performance completed to date.

It was determined that the Group has contracts that meet criteria (a), since the customer simultaneously receives and consumes the benefits provided by the Company's performance as the Company performs. Therefore revenue is recognized over time using the input method based on costs incurred to date as compared to total contract costs. The Company believes that in research and development service type agreements using costs incurred to date represents the most faithful depiction of the entity's performance towards complete satisfaction of a performance obligation.

Revenue from licenses that are not part of a combined performance obligation are recognized at a point in time due to the licenses relating to intellectual property that has significant stand-alone functionality and as such represent a right to use the entity's intellectual property as it exists at the point in time at which the license is granted.

Royalty income received in respect of licensing agreements is recognized as the related third party sales in the licensee occur.

Amounts that are receivable or have been received per contractual terms but have not been recognized as revenue since performance has not yet occurred or has not yet been completed are recorded as deferred revenue. The Company classifies as non-current deferred revenue amounts received for which performance is expected to occur beyond one year or one operating cycle.

Grant Income

The Company recognizes grants from governmental agencies as grant income in the Consolidated Statement of Comprehensive Income/(Loss), gross of the expenditures that were related to obtaining the grant, when there is reasonable assurance that the Company will comply with the conditions within the grant agreement and there is reasonable assurance that payments under the grants will be received. The Company evaluates the conditions of each grant as of each reporting date to ensure that the Company has reasonable assurance of meeting the conditions of each grant arrangement and that it is expected that the grant payment will be received as a result of meeting the necessary conditions.

The Company submits qualifying expenses for reimbursement after the Company has incurred the research and development expense. The Company records an unbilled receivable upon incurring such expenses. In cases were grant income is received prior to the expenses being incurred or recognized, the amounts received are deferred until the related expense is incurred and/or recognized. Grant income is recognized in the Consolidated Statements of Comprehensive Income/(Loss) at the time in which the Company recognizes the related reimbursable expense for which the grant is intended to compensate.

1. Accounting policies — continued

Functional and Presentation Currency

These consolidated financial statements are presented in United States dollars ("US dollars"). The functional currency of virtually all members of the Group is the U.S. dollar. The assets and liabilities of a previously held subsidiary were translated to U.S. dollars at the exchange rate prevailing on the balance sheet date and revenues and expenses were translated at the average exchange rate for the period. Foreign exchange differences resulting from the translation were reported in Other Comprehensive Income/(Loss).

Foreign Currency

Transactions in foreign currencies are translated to the respective functional currencies of Group entities at the foreign exchange rate ruling at the date of the transaction. Monetary assets and liabilities denominated in foreign currencies at the balance sheet date are retranslated to the functional currency at the foreign exchange rate ruling at that date. Foreign exchange differences arising on remeasurement are recognized in the Consolidated Statement of Comprehensive Income/(Loss). Non-monetary assets and liabilities that are measured in terms of historical cost in a foreign currency are translated using the exchange rate at the date of the transaction.

Cash and Cash Equivalents

Cash and cash equivalents include all highly liquid instruments with original maturities of three months or less.

Share Capital

Ordinary shares are classified as equity. The Group is comprised of share capital, share premium, merger reserve, other reserve, translation reserve, and accumulated deficit.

Property and Equipment

Property and equipment is stated at cost less accumulated depreciation and any accumulated impairment losses. Cost includes expenditures that are directly attributable to the acquisition of the asset. Assets under construction represent leasehold improvements and machinery and equipment to be used in operations or research and development activities. When parts of an item of property and equipment have different useful lives, they are accounted for as separate items (major components) of property and equipment. Depreciation is calculated using the straight-line method over the estimated useful life of the related asset:

Laboratory and manufacturing equipment	2-8 years
Furniture and fixtures	7 years
Computer equipment and software	1-5 years
Leasehold improvements	5-10 years, or the remaining term of the lease, if shorter

Depreciation methods, useful lives and residual values are reviewed at each balance sheet date.

Intangible Assets

Intangible assets, which include purchased patents and licenses with finite useful lives, are carried at historical cost less accumulated amortization, if amortization has commenced. Intangible assets with finite lives are amortized from the time they are available for use. Amortization is calculated using the straight-line method to allocate the costs of patents and licenses over their estimated useful lives.

Research and development intangible assets, which are still under development and have accordingly not yet obtained marketing approval, are presented as In-Process Research and Development (IPR&D). IPR&D is not amortized since it is not yet available for its intended use, but it is evaluated for potential impairment on an annual basis or more frequently when facts and circumstances warrant.

Impairment

Impairment of Non-Financial Assets

The Group reviews the carrying amounts of its property and equipment and intangible assets at each reporting date to determine whether there are indicators of impairment. If any such indicators of impairment exist, then an asset's recoverable amount is estimated. The recoverable amount is the higher of an asset's fair value less cost of disposal and value in use.

The Company's IPR&D intangible assets are not yet available for their intended use. As such, they are tested for impairment at least annually.

1. Accounting policies — continued

An impairment loss is recognized when an asset's carrying amount exceeds its recoverable amount. For the purposes of impairment testing, assets are grouped at the lowest levels for which there are largely independent cash flows. If a non-financial asset instrument is impaired, an impairment loss is recognized in the Consolidated Statements of Comprehensive Income/(Loss).

The Company did not record any impairment of such assets during the reported periods.

Investments in associates are considered impaired if, and only if, objective evidence indicates that one or more events, which occurred after the initial recognition, have had an impact on the future cash flows from the net investment and that impact can be reliably estimated. If an impairment exists the Company measures an impairment by comparing the carrying value of the net investment in the associate to its recoverable amount and recording any excess as an impairment loss. See Note 6 for impairment recorded in respect of an investment in associate during the year ended December 31, 2019.

Employee Benefits

Short-Term Employee Benefits

Short-term employee benefit obligations are measured on an undiscounted basis and expensed as the related service is provided. A liability is recognized for the amount expected to be paid if the Group has a present legal or constructive obligation due to past service provided by the employee, and the obligation can be estimated reliably.

Defined Contribution Plans

A defined contribution plan is a post-employment benefit plan under which an entity pays fixed contributions into a separate entity and has no legal or constructive obligation to pay further amounts. Obligations for contributions to defined contribution plans are recognized as an employee benefit expense in the periods during which related services are rendered by employees. Prepaid contributions are recognized as an asset to the extent that a cash refund or a reduction in future payments is available.

Share-based Payments

Share-based payment arrangements, in which the Group receives goods or services as consideration for its own equity instruments, are accounted for as equity-settled share-based payment transactions (except certain restricted stock units – see below) in accordance with IFRS 2, regardless of how the equity instruments are obtained by the Group. The grant date fair value of employee share-based payment awards is recognized as an expense with a corresponding increase in equity over the requisite service period related to the awards. The amount recognized as an expense is adjusted to reflect the actual number of awards for which the related service and non-market performance conditions are expected to be met, such that the amount ultimately recognized as an expense is based on the number of awards that do meet the related service and non-market performance conditions at the vesting date. For share-based payment awards with market conditions, the grant date fair value is measured to reflect such conditions and there is no true-up for differences between expected and actual outcomes.

Certain restricted stock units are treated as liability settled awards starting in 2021. Such awards are remeasured at every reporting date until settlement date and are recognized as compensation expense over the requisite service period. Differences in remeasurement are recognized in profit and loss. The cumulative cost that will ultimately be recognized in respect of these awards will equal to the amount at settlement.

The fair value of the awards is measured using option pricing models and other appropriate models, which take into account the terms and conditions of the awards granted. See further details in Note 8.

Development Costs

Expenditures on research activities are recognized as incurred in the Consolidated Statements of Comprehensive Income/(Loss). In accordance with IAS 38 development costs are capitalized only if the expenditure can be measured reliably, the product or process is technically and commercially feasible, future economic benefits are probable, the Group can demonstrate its ability to use or sell the intangible asset, the Group intends to and has sufficient resources to complete development and to use or sell the asset, and it is able to measure reliably the expenditure attributable to the intangible asset during its development. The point at which technical feasibility is determined to have been reached is, generally, when regulatory approval has been received where applicable. Management determines that commercial viability has been reached when a clear market and pricing point have been identified, which may coincide with achieving meaningful recurring sales. Otherwise, the development expenditure is recognized as incurred in the Consolidated Statements of Comprehensive Income/(Loss). As of balance sheet date the Group has not capitalized any development costs.

1. Accounting policies — continued

Provisions

A provision is recognized in the Consolidated Statements of Financial Position when the Group has a present legal or constructive obligation due to a past event that can be reliably measured, and it is probable that an outflow of economic benefits will be required to settle the obligation. Provisions are determined by discounting the expected future cash flows at a pre-tax rate that reflects risks specific to the liability.

Leases

The Group leases real estate (and some minor equipment) for use in operations. These leases generally have lease terms of 1 to 10 years. The Group includes options that are reasonably certain to be exercised as part of the determination of the lease term. The group determines if an arrangement is a lease at inception of the contract in accordance with guidance detailed in IFRS 16. ROU assets represent the Group's right to use an underlying asset for the lease term and lease liabilities represent our obligation to make lease payments arising from the lease. Operating lease ROU assets and lease liabilities are recognized at commencement date based on the present value of the lease payments over the lease term. As most of our leases do not provide an implicit rate, we use the Group's estimated incremental borrowing rate based on information available at commencement date in determining the present value of future payments.

The Group's operating leases are virtually all leases of real estate.

The Group has elected to account for lease payments as an expense on a straight-line basis over the life of the lease for:

- Leases with a term of 12 months or less and containing no purchase options; and
- Leases where the underlying asset has a value of less than $5,000.

The right-of-use asset is depreciated on a straight-line basis and the lease liability gives rise to an interest charge.

Further information regarding the subleases, right of use asset and lease liability can be found in Note 21.

Finance Income and Finance Costs

Finance income is comprised of income on funds invested in U.S. treasuries, income on money market funds and income on a finance lease. Financing income is recognized as it is earned. Finance costs comprise mainly of loan, notes and lease liability interest expenses and the changes in the fair value of financial liabilities carried at FVTPL (such changes can consist of finance income when the fair value of such financial liabilities decreases).

Taxation

Tax on the profit or loss for the year comprises current and deferred income tax. In accordance with IAS 12, tax is recognized in the Consolidated Statements of Comprehensive Income/(Loss) except to the extent that it relates to items recognized directly in equity.

Current income tax is the expected tax payable or receivable on the taxable income or loss for the year, using tax rates enacted or substantially enacted at the reporting date, and any adjustment to tax payable in respect of previous years.

Deferred tax is recognized due to temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for taxation purposes. Deferred tax assets are recognized for unused tax losses, unused tax credits and deductible temporary differences to the extent that it is probable that future taxable profits will be available against which they can be used. Deferred tax assets with respect to investments in associates are recognized only to the extent that it is probable the temporary difference will reverse in the foreseeable future and taxable profit will be available against which the temporary difference can be utilized. Deferred tax assets are reviewed at each reporting date and are reduced to the extent that it is no longer probable that the related tax benefit will be realized.

Deferred tax is measured at the tax rates that are expected to be applied to temporary differences when they reverse, using tax rates enacted or substantively enacted at the reporting date.

Deferred income tax assets and liabilities are offset when there is a legally enforceable right to offset current tax assets against current tax liabilities and when the deferred income tax assets and liabilities relate to income taxes levied by the same taxation authority on either the same taxable entity or different taxable entities where there is an intention to settle the balances on a net basis.

1. Accounting policies — continued

Fair Value Measurements

The Group's accounting policies require that certain financial assets and certain financial liabilities be measured at their fair value.

The Group uses valuation techniques that are appropriate in the circumstances and for which sufficient data are available to measure fair value, maximizing the use of relevant observable inputs and minimizing the use of unobservable inputs. Fair values are categorized into different levels in a fair value hierarchy based on the inputs used in the valuation techniques as follows:

- Level 1: quoted prices (unadjusted) in active markets for identical assets or liabilities.
- Level 2: inputs other than quoted prices included in Level 1 that are observable for the asset or liability, either directly (i.e. as prices) or indirectly (i.e. derived from prices).
- Level 3: inputs for the asset or liability that are not based on observable market data (unobservable inputs).

The Group recognizes transfers between levels of the fair value hierarchy at the end of the reporting period during which the change has occurred.

The carrying amount of cash and cash equivalents, accounts receivable, restricted cash, deposits, accounts payable, accrued expenses and other current liabilities in the Group's Consolidated Statements of Financial Position approximates their fair value because of the short maturities of these instruments.

Operating Segments

Operating segments are reported in a manner that is consistent with the internal reporting provided to the chief operating decision maker ("CODM"). The CODM reviews discrete financial information for the operating segments in order to assess their performance and is responsible for making decisions about resources allocated to the segments. The CODM has been identified as the Group's Directors.

2. New Standards and Interpretations Not Yet Adopted

A number of new standards, interpretations, and amendments to existing standards are effective for annual periods commencing on or after January 1, 2022 and have not been applied in preparing the consolidated financial information. The Company's assessment of the impact of these new standards and interpretations is set out below.

Effective January 1, 2023, the definition of accounting estimates has been amended as an amendment to IAS 8 Accounting Policies, Changes in Accounting Estimates and Errors. The amendments clarify how companies should distinguish changes in accounting policies from changes in accounting estimates. The distinction is important because changes in accounting estimates are applied prospectively only to future transactions and future events, but changes in accounting policies are generally also applied retrospectively to past transactions and other past events. This amendment is not expected to have an impact on the Group's financial statements.

Effective January 1, 2023, IAS 1 has been amended to clarify that liabilities are classified as either current or non-current, depending on the rights that exist at the end of the reporting period. Classification is unaffected by the expectations of the entity or events after the reporting date. The Company does not expect this amendment will have a material impact on its financial statements.

Effective January 1, 2023, IAS 12 is amended to narrow the scope of the initial recognition exemption (IRE) so that it does not apply to transactions that give rise to equal and offsetting temporary differences. As a result, companies will need to recognise a deferred tax asset and a deferred tax liability for temporary differences arising on initial recognition of a lease and a decommissioning provision. The amendment is not expected to have an impact on the Group's financial statements as the Group has already recognized a deferred tax asset and deferred tax liability that arose on initial recognition of its leases (the Group does not have decommissioning provisions).

None of the other new standards, interpretations, and amendments are applicable to the Company's financial statements and therefore will not have an impact on the Company.

3. Revenue

Revenue recorded in the Consolidated Statement of Comprehensive Income/(Loss) consists of the following:

For the years ended December 31,	**2021 $000s**	2020 $000s	2019 $000s
Contract revenue	**9,979**	8,341	8,688
Grant income	**7,409**	3,427	1,119
Total revenue	**17,388**	11,768	9,807

All amounts recorded in contract revenue were generated in the United States. For the years ended December 31, 2021 and 2020 contract revenue includes royalties received from an associate in the amount of $231 thousand and $54 thousand, respectively.

Primarily all of the Company's contracts in the years ended December 31, 2021, 2020 and 2019 were determined to have a single performance obligation which consists of a combined deliverable of license to intellectual property and research and development services (not including the license acquired by Imbrium upon option exercise – see below). Therefore, for such contracts, revenue is recognized over time based on the input method which the Company believes is a faithful depiction of the transfer of goods and services. Progress is measured based on costs incurred to date as compared to total projected costs. Payments for such contracts are primarily made up front at the inception of the contract (or upon achieving a milestone event) and to a lesser extent payments are made periodically over the contract term.

During the year ended December 31, 2021, the company received a $6.5 million payment from Imbrium Therapeutics, Inc. following the exercise of the option to acquire an exclusive license for the Initial Product Candidate, as defined in the agreement. Since the license transferred was a functional license, revenue from the option exercise was recognized at a point in time upon transfer of the license, which occurred during the year ended December 31, 2021.

During the year ended December 31, 2020, the Company received a $2.0 million milestone payment from Karuna Therapeutics, Inc. following initiation of its KarXT Phase 3 clinical study pursuant to the Exclusive Patent License Agreement between PureTech and Karuna. This milestone was recognized as revenue during the year ended December 31, 2020.

Disaggregated Revenue

The Group disaggregates contract revenue in a manner that depicts how the nature, amount, timing, and uncertainty of revenue and cash flows are affected by economic factors. The Group disaggregates revenue based on contract revenue or grant revenue, and further disaggregates contract revenue based on the transfer of control of the underlying performance obligations.

Timing of contract revenue recognition For the years ended December 31,	**2021 $000s**	2020 $000s	2019 $000s
Transferred at a point in time – Licensing Income[1]	**6,809**	2,054	—
Transferred over time[2]	**3,171**	6,286	8,688
	9,979	8,341	8,688

1 2021 – Attributed to Internal segment ($6.5 million), Controlled Founded Entities segment ($74 thousand) and to Parent Company and Other ($235 thousand); 2020 – Attributed to Parent Company and Other. See note 4, Segment information.

2 2021 – Attributed to Internal segment ($1,629 thousand) and Controlled Founded Entities segment ($1,541 thousand); 2020 – Attributed to Internal segment ($5,297 thousand), and Controlled Founded Entities segment ($990 thousand), 2019 – Attributed to Internal segment ($7,077 thousand), Controlled founded entities segment ($1,474 thousand) and Parent Company and Other ($137 thousand). See Note 4, Segment Information.

3. Revenue — continued

Customers over 10% of revenue	**2021 $000s**	2020 $000s	2019 $000s
Customer A	**—**	1,518	4,973
Customer B	**1,500**	896	1,433
Customer C	**—**	2,043	1,091
Customer D	**7,250**	1,736	1,013
Customer E	**—**	2,000	—
	8,750	8,193	8,510

Accounts receivables represent rights to consideration in exchange for products or services that have been transferred by the Group, when payment is unconditional and only the passage of time is required before payment is due. Accounts receivables do not bear interest and are recorded at the invoiced amount. Accounts receivable are included within Trade and other receivables on the Consolidated Statement of Financial Position.

Contract liabilities represent the Group's obligation to transfer products or services to a customer for which consideration has been received, or for which an amount of consideration is due from the customer. Contract liabilities are included within deferred revenue on the Consolidated Statement of Financial Position.

Contract Balances	**2021 $000s**	2020 $000s
Accounts receivable	**704**	711
Deferred revenue – short term	**65**	1,472

During the year ended December 31, 2021, $1.4 million of revenue was recognized from deferred revenue outstanding at December 31, 2020.

Remaining performance obligations represent the transaction price of unsatisfied or partially satisfied performance obligations within contracts with an original expected contract term that is greater than one year and for which fulfillment of the contract has started as of the end of the reporting period. The aggregate amount of transaction consideration allocated to remaining performance obligations as of December 31, 2021, was nil.

4. Segment Information

Basis for Segmentation

The Directors are the Group's strategic decision-makers. The Group's operating segments are reported based on the financial information provided to the Directors periodically for the purposes of allocating resources and assessing performance. The Group has determined that each entity is representative of a single operating segment as the Directors monitor the financial results at this level. When identifying the reportable segments the Group has determined that it is appropriate to aggregate multiple operating segments into a single reportable segment given the high level of operational and financial similarities across the entities.

The Group has identified multiple reportable segments as presented below. There was no change to reportable segments in 2021, except the change in the composition of the segments with respect to Alivio, as explained below. Virtually all of the revenue and profit generating activities of the Group are generated within the United States and accordingly, no geographical disclosures are provided.

During the year ended December 31, 2021, the Company acquired the non-controlling interest in Alivio and since then Alivio is wholly owned by the Company and is managed within the Internal segment. The Company has revised in these financial statements the prior period financial information to conform to the presentation as of and for the period ending December 31, 2021. The change in segments reflects how the Company's Board of Directors reviews the Group's results, allocates resources and assesses performance of the Group at this time.

Internal

The Internal segment (the "Internal segment"), is advancing Wholly Owned Programs which is focused on immunological, fibrotic and lymphatic system disorders and builds upon validated biologic pathways and proven pharmacology. The Internal segment is comprised of the technologies that are wholly owned and will be advanced through either PureTech Health funding or non-dilutive sources of financing in the near-term. The operational management of the Internal segment is conducted by the PureTech Health team, which is responsible for the strategy, business development, and research and development. As of December 31, 2021, this segment included PureTech LYT (formerly Ariya Therapeutics), PureTech LYT-100 and Alivio Therapeutics, Inc.

Controlled Founded Entities

The Controlled Founded Entity segment (the "Controlled Founded Entity segment") is comprised of the Group's subsidiaries that are currently consolidated operational subsidiaries that either have, or have plans to hire, independent management teams and currently have already raised third-party dilutive capital. These subsidiaries have active research and development programs and either have entered into or plan to seek an equity or debt investment partner, who will provide additional industry knowledge and access to networks, as well as additional funding to continue the pursued growth of the company. As of December 31, 2021, this segment included Entrega Inc., Follica Incorporated, Sonde Health Inc., and Vedanta Biosciences, Inc.

Non-Controlled Founded Entities

The Non-Controlled Founded Entities segment (the "Non-Controlled Founded Entities segment") is comprised of the entities in respect of which PureTech Health (i) no longer holds majority voting control as a shareholder and no longer has the right to elect a majority of the members of the subsidiaries' Board of Directors. Upon deconsolidation of an entity the segment disclosure is restated to reflect the change on a retrospective basis, as this constitutes a change in the composition of its reportable segments. The Non-Controlled Founded Entities segment includes Vor Biopharma Inc. ("Vor"), Karuna Therapeutics, Inc. ("Karuna"), and Gelesis Inc. ("Gelesis"), which were deconsolidated during the year ended December 31, 2019.

The Non-Controlled Founded Entities segment incorporates the operational results of the aforementioned entities to the date of deconsolidation. Following the date of deconsolidation, the Company accounts for its investment in each entity at the parent level, and therefore the results associated with investment activity following the date of deconsolidation is included in the Parent Company and Other section.

Parent Company and Other

Parent Company and Other includes activities that are not directly attributable to the operating segments, such as the activities of the Parent, corporate support functions and certain research and development support functions that are not directly attributable to a strategic business segment as well as the elimination of intercompany transactions. Intercompany transactions between segments consist primarily of management fees charged from the Parent Company to the other segments. This section also captures the accounting for the Company's holdings in entities for which control has been lost, which is inclusive of the following items: gain on deconsolidation, gain or loss on investments held at fair value, gain on loss of significant influence, and the share of net income/ (loss) of associates accounted for using the equity method. As of December 31, 2021, this segment included PureTech Health plc, PureTech Health LLC, PureTech Management, Inc., PureTech Securities Corp. and PureTech Securities II Corp., as well as certain other dormant, inactive and shell entities.

4. Segment Information — continued

Information About Reportable Segments:

	2021				
	Internal $000s	Controlled Founded Entities $000s	Non-Controlled Founded Entities $000s	Parent Company & Other $000s	Consolidated $000s
Consolidated Statements of Comprehensive Income/(Loss)					
Contract revenue	**8,129**	**1,615**	**—**	**235**	**9,979**
Grant revenue	**1,253**	**6,156**	**—**	**—**	**7,409**
Total revenue	**9,382**	**7,771**	**—**	**235**	**17,388**
General and administrative expenses	**(8,673)**	**(20,729)**	**—**	**(27,797)**	**(57,199)**
Research and development expenses	**(65,444)**	**(43,783)**	**—**	**(1,244)**	**(110,471)**
Total operating expense	**(74,118)**	**(64,512)**	**—**	**(29,041)**	**(167,671)**
Other income/(expense):					
Gain/(loss) on investments held at fair value	**—**	**—**	**—**	**179,316**	**179,316**
Loss realized on sale of investments	**—**	**—**	**—**	**(20,925)**	**(20,925)**
Gain/(loss) on disposal of assets	**(1)**	**(51)**	**—**	**—**	**(53)**
Other income/(expense)	**—**	**121**	**—**	**1,523**	**1,645**
Total other income/(expense)	**(1)**	**70**	**—**	**159,914**	**159,983**
Net finance income/(costs)	**(16)**	**6,744**	**—**	**(1,679)**	**5,050**
Share of net income/(loss) of associates accounted for using the equity method	**—**	**—**	**—**	**(73,703)**	**(73,703)**
Income/(loss) before taxes	**(64,753)**	**(49,927)**	**—**	**55,727**	**(58,953)**
Income/(loss) before taxes pre IFRS 9 fair value accounting, finance costs – subsidiary preferred shares, share-based payment expense, depreciation of tangible assets and amortization of intangible assets	**(60,368)**	**(50,583)**	**—**	**63,628**	**(47,323)**
Finance income/(costs) – IFRS 9 fair value accounting	**—**	**9,606**	**—**	**—**	**9,606**
Share-based payment expense	**(3,066)**	**(6,256)**	**—**	**(4,628)**	**(13,950)**
Depreciation of tangible assets	**(1,319)**	**(1,518)**	**—**	**(1,510)**	**(4,347)**
Amortization of ROU assets	**—**	**(1,174)**	**—**	**(1,764)**	**(2,938)**
Amortization of intangible assets	**—**	**(2)**	**—**	**—**	**(2)**
Taxation	**—**	**—**	**—**	**(3,756)**	**(3,756)**
Income/(loss) for the year	**(64,753)**	**(49,927)**	**—**	**51,971**	**(62,709)**
Other comprehensive income/(loss)	**—**	**—**	**—**	**—**	**—**
Total comprehensive income/(loss) for the year	**(64,753)**	**(49,927)**	**—**	**51,971**	**(62,709)**
Total comprehensive income/(loss) attributable to:					
Owners of the Company	**(64,657)**	**(47,857)**	**—**	**51,956**	**(60,558)**
Non-controlling interests	**(96)**	**(2,069)**	**—**	**15**	**(2,151)**
	December 31, 2021 $000s				
Consolidated Statements of Financial Position:					
Total assets	**125,726**	**66,274**	**—**	**754,007**	**946,006**
Total liabilities[1]	**228,789**	**228,857**	**—**	**(95,787)**	**361,859**
Net assets/(liabilities)	**(103,063)**	**(162,584)**	**—**	**849,794**	**584,147**

1 Parent Company and Other Includes eliminations of intercompany liabilities between the Parent Company and the reportable segments in the amount of $233.3 million.

4. Segment Information — continued

	2020				
	Internal $000s	Controlled Founded Entities $000s	Non-Controlled Founded Entities $000s	Parent Company & Other $000s	Consolidated $000s
Consolidated Statements of Comprehensive Income/(Loss)					
Contract revenue	5,297	990	—	2,054	8,341
Grant revenue	1,563	1,864	—	—	3,427
Total revenue	6,860	2,853	—	2,054	11,768
General and administrative expenses	(3,482)	(13,691)	—	(32,267)	(49,440)
Research and development expenses	(45,346)	(36,279)	—	(234)	(81,859)
Total Operating expenses	(48,828)	(49,970)	—	(32,500)	(131,299)
Other income/(expense):					
Gain/(loss) on investments held at fair value	—	—	—	232,674	232,674
Loss realized on sale of investments	—	—	—	(54,976)	(54,976)
Gain/(loss) on disposal of assets	(15)	(15)	—	—	(30)
Other income/(expense)	—	100	—	965	1,065
Other income/(expense)	(15)	85	—	178,662	178,732
Net finance income/(costs)	19	(5,204)	—	(930)	(6,115)
Share of net income/(loss) of associate accounted for using the equity method	—	—	—	(34,117)	(34,117)
Income/(loss) before taxes	(41,964)	(52,236)	—	113,170	18,969
(Loss)/income before taxes pre IFRS 9 fair value accounting, finance costs – subsidiary preferred shares, share-based payment expense, depreciation of tangible assets and amortization of intangible assets	(38,349)	(42,602)	—	121,644	40,694
Finance income/(costs) – subsidiary preferred shares	—	—	—	—	—
Finance income/(costs) – IFRS 9 fair value accounting	—	(4,351)	—	—	(4,351)
Share-based payment expense	(2,762)	(2,552)	—	(5,405)	(10,718)
Depreciation of tangible assets	(854)	(1,544)	—	(1,547)	(3,945)
Amortization of ROU assets	—	(1,186)	—	(1,523)	(2,709)
Amortization of intangible assets	—	(1)	—	—	(1)
Taxation	—	(1)	—	(14,400)	(14,401)
Income/(loss) for the year	(41,964)	(52,237)	—	98,769	4,568
Other comprehensive income/(loss)	—	—	—	469	469
Total comprehensive income/(loss) for the year	(41,964)	(52,237)	—	99,238	5,037
Total comprehensive income/(loss) attributable to:					
Owners of the Company	(41,773)	(51,026)	—	99,253	6,454
Non-controlling interests	(191)	(1,211)	—	(15)	(1,417)
	December 31, 2020 $000s				
Consolidated Statements of Financial Position:					
Total assets	89,214	67,433	—	833,347	989,994
Total liabilities	130,049	200,457	—	5,949	336,455
Net (liabilities)/assets	(40,835)	(133,023)	—	827,397	653,539

The proportion of net assets shown above that is attributable to non-controlling interest is disclosed in Note 18.

4. Segment Information — continued

	2019				
	Internal $000s	Controlled Founded Entities $000s	Non-Controlled Founded Entities $000s	Parent Company & Other $000s	Consolidated $000s
Consolidated Statements of Comprehensive Loss					
Contract revenue	7,077	1,474	—	137	8,688
Grant revenue	928	191	—	—	1,119
Total revenue	8,006	1,664	—	137	9,807
General and administrative expenses	(3,252)	(13,569)	(10,439)	(32,098)	(59,358)
Research and development expenses	(28,874)	(39,883)	(15,555)	(1,536)	(85,848)
Total operating expense	(32,126)	(53,451)	(25,994)	(33,634)	(145,206)
Other income/(expense):					
Gain on deconsolidation	—	—	—	264,409	264,409
Gain/(loss) on investments held at fair value	—	—	—	(37,863)	(37,863)
Gain/(loss) on disposal of assets	17	(39)	—	(60)	(82)
Gain on loss of significant influence	—	—	—	445,582	445,582
Other income/(expense)	—	166	—	(45)	121
Other income/(expense)	17	127	—	672,023	672,167
Net finance income/(costs)	—	(16,947)	(30,141)	941	(46,147)
Share of net income/(loss) of associate accounted for using the equity method	—	—	—	30,791	30,791
Impairment of investment in associate	—	—	—	(42,938)	(42,938)
Income/(loss) before taxes	(24,104)	(68,608)	(56,135)	627,320	478,474
(Loss)/income before taxes pre IAS 39 fair value accounting, finance costs – subsidiary preferred shares, share-based payment expense, depreciation of tangible assets and amortization of intangible assets	(23,698)	(47,188)	(21,873)	640,298	547,540
Finance income/(costs) – subsidiary preferred shares	—	107	(1,564)	(1)	(1,458)
Finance income/(costs) – IFRS 9 fair value accounting	—	(17,294)	(28,737)	(444)	(46,475)
Share-based payment expense	(19)	(1,664)	(3,543)	(9,242)	(14,468)
Depreciation of tangible assets	(390)	(1,517)	(207)	(1,114)	(3,228)
Amortization of ROU assets	—	(1,060)	(83)	(2,177)	(3,320)
Amortization of intangible assets	4	7	(128)	—	(117)
Taxation	—	(134)	(162)	(112,113)	(112,409)
Income/(loss) for the year	(24,104)	(68,741)	(56,297)	515,207	366,065
Other comprehensive income/(loss)	—	—	(10)	—	(10)
Total comprehensive income/(loss) for the year	(24,104)	(68,741)	(56,307)	515,207	366,055
Total comprehensive income/(loss) attributable to:					
Owners of the Company	(6,461)	(55,258)	(32,353)	515,207	421,133
Non-controlling interests	(17,643)	(13,483)	(23,953)	—	(55,079)

5. Investments held at fair value

Investments held at fair value include both unlisted and listed securities held by PureTech. These investments, which include interests in Akili, Vor, Karuna, Gelesis (other than the investment in common shares which is accounted for under the equity method), and other insignificant investments, are initially measured at fair value and are subsequently re-measured at fair value at each reporting date with changes in the fair value recorded through profit and loss. Interests in these investments were accounted for as shown below:

Investments held at fair value	$000's
Balance as of January 1, 2020	714,905
Sale of Karuna shares	(347,538)
Sale of resTORbio shares	(3,048)
Loss realised on sale of investments	(54,976)
Cash purchase of Gelesis preferred shares (please refer to Note 6)	10,000
Cash purchase of Vor preferred shares	1,150
Unrealized Loss – fair value through profit and loss	232,674
Balance as of January 1, 2021 before allocation of share in associate loss to long-term interest	553,167
Sale of Karuna shares	(218,125)
Loss realised on sale of investments (see below)	(20,925)
Cash purchase of Vor preferred shares	500
Unrealized gain – fair value through profit and loss	179,271
Balance as of December 31, 2021 before allocation of share in associate loss to long-term interest	**493,888**
Share of associate loss allocated to long-term interest (see Note 6)	(96,709)
Balance as of December 31, 2021 after allocation of share in associate loss to long-term interest[1]	**397,179**

1 Fair value of investments accounted for at fair value, does not take into consideration contribution from milestones that occurred after December 31, 2021, the value of the Group's consolidated Founded Entities (Vedanta, Follica, Sonde and Entrega), the Internal segment, or cash and cash equivalents.

Vor

On February 12, 2019, Vor completed a Series A-2 Preferred Shares financing round with PureTech and several new third party investors. The financing provided for the purchase of 62,819,866 shares of Vor Series A-2 Preferred Shares at the purchase price of $0.40 per share.

As a result of the issuance of Series A-2 preferred shares to third-party investors, PureTech's ownership percentage and corresponding voting rights dropped from 79.5 percent to 47.5 percent, and PureTech simultaneously lost control on Vor's Board of Directors, both of which triggered a loss of control over the entity. As of February 12, 2019, Vor was deconsolidated from the Group's financial statements, resulting in only the profits and losses generated by Vor through the deconsolidation date being included in the Consolidated Statement of Comprehensive Income/(Loss). While the Company no longer controlled Vor, it was concluded that PureTech still had significant influence over Vor by virtue of its large, albeit minority, ownership stake and its continued representation on Vor's Board of Directors. During the year ended December 31, 2019, the Company recognized a $6.4 million gain on the deconsolidation of Vor, which was recorded to the Gain on the deconsolidation of subsidiary line item in the Consolidated Statement of Comprehensive Income/(Loss).

As PureTech did not hold common shares in Vor upon deconsolidation and the preferred shares it held did not have equity-like features, PureTech had no basis to account for its investment in Vor under IAS 28. The preferred shares held by PureTech fell under the guidance of IFRS 9 and were treated as a financial asset held at fair value with changes in fair value recorded in the Consolidated Statement of Comprehensive Income/(Loss). The fair value of the preferred shares at deconsolidation was $12.0 million.

On February 12, 2020, PureTech participated in the second closing of Vor's Series A-2 Preferred Share financing. For consideration of $0.7 million, PureTech received 1,625,000 A-2 shares. On June 30, 2020, PureTech participated in the first closing of Vor's Series B Preferred Share financing. For consideration of $0.5 million, PureTech received 961,538 shares. Upon the conclusion of such Vor financings PureTech no longer had significant influence over Vor.

On January 8, 2021, PureTech participated in the second closing of Vor's Series B Preferred Share financing. For consideration of $0.5 million, PureTech received an additional 961,538 B Preferred shares.

On February 9, 2021, Vor closed its initial public offering (IPO) of 9,828,017 shares of its common stock at a price to the public of $18.00 per share. Subsequent to the closing, PureTech held 3,207,200 shares of Vor common stock, representing 8.6 percent of Vor common stock. Following its IPO, the valuation of Vor common stock is based on level 1 inputs in the fair value hierarchy. See Note 16.

During the years ended December 31, 2021, 2020 and 2019, the Company recognized a gain of $3.9 million, a gain of $19.1 million, and a gain of $0.6 million, respectively for the changes in the fair value of the investment that were recorded in the line item Gain/(loss) on investments held at fair value within the Consolidated Statement of Comprehensive Income/(Loss). Please refer to Note 16 for information regarding the valuation of these instruments.

5. Investments held at fair value — continued

Gelesis

As of July 1, 2019, Gelesis was deconsolidated from the Group's financial statements, resulting in only the profits and losses generated by Gelesis through the deconsolidation date being included in the Group's Consolidated Statement of Income/(Loss). At the date of deconsolidation, PureTech recorded a $156.0 million gain on the deconsolidation of Gelesis, which was recorded to the Gain on the deconsolidation of subsidiary line item in the Consolidated Statement of Income/(Loss). The preferred shares and warrants held by PureTech fall under the guidance of IFRS 9 and are treated as financial assets held at fair value, where changes to the fair value of the preferred shares and warrant are recorded through the Consolidated Statement of Income/(Loss). The fair value of the preferred shares and warrants at deconsolidation was $49.2 million. Please refer to Note 6 for information regarding the Company's investment in Gelesis as an associate.

On August 12, 2019, Gelesis issued a convertible promissory note to the Company in the amount of $2.0 million. On October 7, 2019, Gelesis issued an amended and restated convertible note (the "Gelesis Note") to the Company in the principal amount of up to $6.5 million. The Gelesis Note was payable in installments, with $2.0 million of the note drawn down upon execution of the original note in August 2019 and an additional $3.3 million and $1.2 million drawn down on October 7, 2019 and November 5, 2019, respectively. The Gelesis Note was convertible upon the occurrence of Gelesis' next qualified equity financing, or at the demand of the Company at any date after December 31, 2019. The Gelesis Note fell under the guidance of IFRS 9 and was treated as a financial asset held at fair with all movements to the value of the note recorded through the Consolidated Statement of Income/(Loss).

On December 5, 2019, Gelesis closed its Series 3 Growth Preferred Stock financing, at which point all outstanding principal and interest under the Gelesis Note converted into shares of Series 3 Growth Preferred Stock. In addition to the shares issued upon conversion of the Gelesis Note, PureTech purchased $8.0 million of Series 3 Growth Preferred Stock in the December financing.

On April 1, 2020, PureTech participated in the 2nd closing of Gelesis's Series 3 Growth Preferred Share financing. For consideration of $10.0 million, PureTech received 579,038 Series 3 Growth shares.

During the years ended December 31, 2021, 2020 and 2019, the Company recognized a gain of $34.6 million, a gain of $7.1 million and a loss of $18.7 million, respectively related to the change in the fair value of the preferred shares and warrants that was recorded in the line item Gain/(loss) on investments held at fair value within the Consolidated Statement of Comprehensive Income/(Loss). The loss recorded in 2019 was primarily as a result of the Gelesis Series 3 Growth financing, which was executed with terms that resulted in a decrease in fair value across all other classes of preferred shares. Please refer to Note 16 for information regarding the valuation of these instruments. Additionally, due to the equity method based investment in Gelesis being reduced to zero, the Group allocated a portion of its share in the net loss in Gelesis in the years ended December 31, 2021 and 2020, totaling $73.7 million and $23.0 million, respectively, to its preferred share and warrant investments in Gelesis, which are considered to be long-term interests in Gelesis. As of December 31, 2021, the investment in Gelesis preferred shares and warrants was entirely reduced to nil.

See Note 26 for subsequent event regarding the investment in Gelesis.

Karuna

2019

On March 15, 2019, Karuna completed the closing of a Series B Preferred Share financing with PureTech and several new third party investors. The financing provided for the purchase of 5,285,102 shares of Karuna Series B Preferred Shares at a purchase price of $15.14 per share.

As a result of the issuance of the preferred shares to third-party investors, PureTech's ownership percentage and corresponding voting rights related to Karuna dropped from 70.9 percent to 44.3 percent, and PureTech simultaneously lost control over Karuna's Board of Directors, both of which triggered a loss of control over the entity. As of March 15, 2019, Karuna was deconsolidated from the Group's financial statements, resulting in only the profits and losses generated by Karuna through the deconsolidation date being included in the Group's Consolidated Statement of Comprehensive Income/(Loss). At the date of deconsolidation, PureTech recorded a $102.0 million gain on the deconsolidation of Karuna, which was recorded to the Gain on the deconsolidation of subsidiary line item in the Consolidated Statement of Comprehensive Income/(Loss). While the Company no longer controls Karuna, it was concluded that PureTech still had significant influence over Karuna by virtue of its large, albeit minority, ownership stake and its continued representation on Karuna's Board of Directors. As PureTech had significant influence over Karuna, the entity was accounted for as an associate under IAS 28.

Upon the date of deconsolidation, PureTech held both preferred and common shares in Karuna and a warrant issued by Karuna to PureTech. The preferred shares and warrant held by PureTech fell under the guidance of IFRS 9 and were treated as financial assets held at fair value, and all movements to the value of preferred shares held by PureTech were recorded through the Consolidated Statement of Comprehensive Income/(Loss), in accordance with IFRS 9. The fair value of the preferred shares and warrant at deconsolidation was $72.4 million. Subsequent to deconsolidation, PureTech purchased an additional $5.0 million of Karuna Series B Preferred shares.

Due to the immaterial investment in common shares and overwhelmingly large losses by Karuna, the common share investment accounted for under the equity method was remeasured to nil immediately following both the deconsolidation and the exercise of the warrant in the first half of 2019.

5. Investments held at fair value — continued

On June 28, 2019, Karuna priced its IPO. PureTech's ownership percentage and corresponding voting rights related to Karuna dropped from 44.3 percent percent to 31.6 percent; however, PureTech retained significant influence due to its continued presence on the board and its large, albeit minority, equity stake in the company. Upon completion of the IPO, the Karuna preferred shares held by PureTech converted to common shares. In light of PureTech's common share holdings in Karuna and corresponding voting rights, PureTech had re-established a basis to account for its investment in Karuna under IAS 28. The preferred shares investment held at fair value was therefore reclassified to investment in associate upon completion of the conversion. During the year ended December 31, 2019 and up to June 28, 2019, the Company recognized a gain of $40.6 million that was recorded on the line item Gain on investments held at fair value within the Consolidated Statement of Comprehensive Income/(Loss) related to the preferred shares that increased in value between the date of deconsolidation and the date of Karuna's IPO.

As of December 2, 2019 it was concluded that the Company no longer exerted significant influence over Karuna owing to the resignation of the PureTech designee from Karuna's Board of Directors, with PureTech retaining no ability to reappoint representation. Furthermore, PureTech was not involved in any manner, or had any influence, on the management of Karuna, or on any of its decision making processes and had no ability to do so. As such, PureTech lost the power to participate in the financial and operating policy decisions of Karuna. As a result, Karuna was no longer deemed an Associate and did not meet the scope of equity method accounting, resulting in the investment being accounted for as an investment held at fair value. As of December 2, 2019 the Company's interest in Karuna was 28.4 percent. For the period of June 28, 2019 through December 2, 2019, PureTech's investment in Karuna was subject to equity method accounting. In accordance with IAS 28, the Company's investment was adjusted by the share of losses generated by Karuna (weighted average of 31.4 percent based on common stock ownership interest), which resulted in a net loss of associates accounted for using the equity method of $6.3 million during the year ended December 31, 2019.

Upon PureTech's loss of significant influence, the investment in Karuna was reclassified to an investment held at fair value. This change led PureTech to recognize a gain on loss of significant influence of $445.6 million that was recorded to the Consolidated Statement of Comprehensive Income/(Loss) on the line item Gain on loss of significant influence during the year ended December 31, 2019. The investment in Karuna after the recording of the gain on loss of significant influence was $557.2 million, which was reclassified from Investments in associates to Investments held at fair value. Additionally, from December 2, 2019 PureTech recorded a $0.7 million loss on the line item Gain/(loss) on investments held at fair value within the Consolidated Statement of Comprehensive Income/(Loss) for the year ended December 31, 2019.

2020 and 2021

On January 22, 2020, PureTech sold 2,100,000 shares of Karuna common shares for aggregate proceeds of $200.9 million. On May 26, 2020, PureTech sold an additional 555,500 Karuna common shares for aggregate proceeds of $45.0 million. On August 26, 2020, PureTech sold 1,333,333 common shares of Karuna for aggregate proceeds of $101.6 million. As a result of the sales, Puretech recorded a loss of $54.8 million attributable to blockage discount included in the sales price, to the line item Loss Realized on Sale of Investment within the Consolidated Statement of Comprehensive Income/(Loss). See below for gain recorded in respect of the change in fair value of the Karuna investment.

On February 9, 2021, the Group sold 1,000,000 common shares of Karuna for $118.0 million. Following the sale the Group held 2,406,564 common shares of Karuna, which represented 8.2 percent of Karuna common stock at the time of sale. On November 9, 2021, the group sold an additional 750,000 common shares of Karuna for $100.1 million. Following the sale the group holds 1,656,564 common shares of Karuna, which represented 5.6 percent at time of sale. As a result of the aforementioned sales, the Company recorded a loss of $20.9 million, attributable to blockage discount included in the sales price, to the line item Loss Realised on Sale of Investment within the Consolidated Statement of Comprehensive Income/(Loss) for the year ended December 31, 2021. See below for gain recorded in respect of the change in fair value of the Karuna investment.

During the years ended December 31, 2021 and 2020, the Company recognized a gain of $110.0 million and a gain of $191.2 million, respectively for the changes in the fair value of the Karuna investment that were recorded in the line item Gain/(loss) on investments held at fair value within the Consolidated Statement of Comprehensive Income/(Loss). As of December 31, 2021, PureTech continued to hold Karuna common shares or 5.6 percent of total outstanding Karuna common shares. Please refer to Note 16 for information regarding the valuation of these instruments.

Akili

As PureTech does not hold common shares in Akili and the preferred shares it holds do not have equity-like features, PureTech has no basis to account for its investment in Akili under IAS 28. The preferred shares held by PureTech Health fall under the guidance of IFRS 9 and are treated as a financial asset held at fair value and all movements to the value of the preferred shares are recorded through the Consolidated Statements of Comprehensive Income/(Loss), in accordance with IFRS 9.

On May 25, 2021, Akili completed its Series D financing for gross proceeds of $110.0 million in which Akili issued 13,053,508 Series D preferred shares. The Group did not participate in this round of financing and as a result, the Group's interest in Akili was reduced from 41.9 percent to 27.5 percent.

During the years ended December 31, 2021, 2020 and 2019, the Company recognized a gain of $32.2 million, a gain of $14.4 million, and a gain of $11.5 million, respectively for the changes in the fair value of the investment in Akili that was recorded on the line item Gain/(loss) on investments held at fair value within the Consolidated Statement of Comprehensive Income/(Loss). Please refer to Note 16 for information regarding the valuation of these instruments.

5. Investments held at fair value — continued

resTORbio

On November 15, 2019, resTORbio announced that top line data from the Protector 1 Phase 3 study evaluating the safety and efficacy of RTB101 in preventing clinically symptomatic respiratory illness in adults age 65 and older, did not meet its primary endpoint and the Company has stopped the development of RTB101 in this indication. As a result of ceasing the development of RTB101, resTORbio's share price witnessed a decline in price. In November and December 2019, PureTech Health sold 7,680,700 common shares of resTORbio for aggregate proceeds of $9.3 million. Immediately following the sale of common shares, PureTech Health held 2,119,696 common shares, or 5.8 percent, of resTORbio. During the year ended December 31, 2019 PureTech recorded a loss of $71.9 million for the adjustment to fair value of its investment in resTORbio to the Consolidated Statement of Comprehensive Income/(Loss) in the line item Gain/(loss) on investments held at fair value.

On April 30, 2020, PureTech sold its remaining 2,119,696 resTORbio common shares, for aggregate proceeds of $3.0 million. As a result of the sale, the Company recorded a loss of $0.2 million attributable to blockage discount included in the sales price, to the line item Loss realized on sale of investments within the Consolidated Statement of Comprehensive Income/(Loss). Additionally, during the year ended December 31, 2020, the Company recognized a gain of $0.1 million that was recorded on the line item Gain/(loss) on investments held at fair value within the Consolidated Statement of Comprehensive Income/(Loss).

Gain on deconsolidation

The following table summarizes the gain on deconsolidation recognized by the Company:

Year ended December 31,	**2021 $000s**	2020 $000s	2019 $000s
Gain on deconsolidation of Vor	**—**	—	6,357
Gain on deconsolidation of Karuna	**—**	—	102,038
Gain on deconsolidation of Gelesis [Note 6]	**—**	—	156,014
Total gain on deconsolidation	**—**	—	264,409

6. Investments in Associates

Gelesis

Gelesis was founded by PureTech and raised funding through preferred shares financings as well as issuances of warrants and loans. As of January 1, 2019, PureTech maintained control of Gelesis and Gelesis's financial results were fully consolidated in the Group's consolidated financial statements.

On July 1, 2019, the Gelesis Board of Directors was restructured, resulting in two of the three PureTech representatives resigning from the Board with PureTech retaining no ability to reappoint Directors to these board seats. As a result of this restructuring, PureTech lost control over Gelesis' Board of Directors, which triggered a loss of control over the entity. At the deconsolidation date, PureTech held a 25.2 percent voting interest in Gelesis. As of July 1, 2019, Gelesis was deconsolidated from the Group's financial statements, resulting in only the profits and losses generated by Gelesis through the deconsolidation date being included in the Group's Consolidated Statement of Income/(Loss) and Other Comprehensive Income/(Loss). At the date of deconsolidation, PureTech recorded a $156.0 million gain on the deconsolidation of Gelesis, which was recorded to the Gain on the deconsolidation of subsidiary line item in the Consolidated Statement of Comprehensive Income/(Loss). While the Company no longer controls Gelesis, it was concluded that PureTech still has significant influence over Gelesis by virtue of its large, albeit minority, ownership stake and its continued representation on Gelesis' Board of Directors and as such Gelesis is accounted for as an associate under IAS 28, starting at the date of deconsolidation.

Upon the date of deconsolidation, PureTech held preferred shares and common shares of Gelesis and a warrant issued by Gelesis to PureTech. PureTech's investment in common shares of Gelesis is subject to equity method accounting with an initial investment of $16.4 million. In accordance with IAS 28, PureTech's investment was adjusted by the share of profits and losses generated by Gelesis subsequent to the date of deconsolidation. See table below for the Group's share in the profits and losses of Gelesis for the periods presented.

The preferred shares and warrant held by PureTech fall under the guidance of IFRS 9 and are treated as financial assets held at fair value, where changes to the fair value of the preferred shares and warrant are recorded through the Consolidated Statement of Income/(Loss) and Other Comprehensive Income/(Loss), in accordance with IFRS 9. The fair value of the preferred shares and warrant at deconsolidation was $49.2 million. See Note 5 for changes in the fair value subsequent to deconsolidation date.

6. Investments in Associates — continued

Impairment loss for the year ended December 31, 2019

Following the issuance of the Gelesis Series 3 Preferred Shares at a higher valuation than the previous round with some favorable liquidation provisions primarily to PureTech and also to the other Series 3 preferred share investors, which resulted in adjustments to the fair values of other preferred shares, warrant classes and Gelesis common stock, the Company assessed the investment in common shares held in Gelesis for impairment. Management compared the recoverable amount of the investment to its carrying amount as of December 31, 2019, which resulted in an impairment loss to the Investment in Gelesis. The recoverable amount was estimated based on the fair value of the Gelesis common shares held by PureTech, which are considered to be within Level 3 of the fair value hierarchy. The costs of disposal are immaterial for the calculation of Gelesis investment's recoverable amount. The total fair value of common shares was determined utilizing a hybrid valuation approach with significant unobservable inputs within the PureTech valuation framework. The multi-scenario hybrid valuation approach utilized the recent transaction method within an option pricing framework and an IPO scenario within a probability-weighted-expected return framework to determine the value allocation for the common share class of Gelesis. The PWERM maintained a 75.0 percent probability of occurrence while the OPM maintained a 25.0 percent probability of occurrence. The probability weighted term to exit was 1.57 years. The discount rate utilized was 20.0 percent while the risk-free rate and volatility utilized were 1.62 percent and 56.0 percent, respectively.

The impairment loss amounted to $42.9 million and was recorded to Impairment of investment in associate within the Consolidated Statement of Comprehensive Income/(Loss) for the year ended December 31, 2019. As of December 31, 2019 the investment in Gelesis was $10.6 million, which is equal to the fair value of the common shares held by PureTech.

Years ended December 31, 2020 and 2021

During the year ended December 31, 2021 and 2020, the Group recorded its share in the losses of Gelesis. In 2020 the Group's investment in associates accounted for under the equity method was reduced to zero. Since the Group has investments in Gelesis warrants and preferred shares that are deemed to be Long-term interests, the Company continued recognizing its share in Gelesis losses while applying such losses to its preferred share and warrant investment in Gelesis accounted for as an investment held at fair value. In 2021, the total investment in Gelesis, including the Long-term interests, was reduced to zero. Since the Group did not incur legal or constructive obligations or made payments on behalf of Gelesis, the Group discontinued recognizing equity method losses. As of December 31, 2021, unrecognized equity method losses amounted to $38.1 million, which included $0.7 million of unrecognized other comprehensive loss.

During 2021, due to exercise of stock options into common shares in Gelesis the Group's equity interest in Gelesis was reduced from 47.9 percent at December 31, 2020 to 42.0 percent as of December 31, 2021. The gain resulting from the issuance of shares to third parties and the resulting reduction in the Group's share in the accumulated deficit of Gelesis under the equity method was fully offset by the unrecognized equity method losses.

Karuna

For the period of June 28, 2019, through December 2, 2019, PureTech's investment in Karuna was subject to equity method accounting. In accordance with IAS 28, the Company's investment was adjusted by the share of losses generated by Karuna (weighted average of 31.4 percent based on common stock ownership interest), which resulted in a net loss of $6.3 million during the year ended December 31, 2019, recorded in the line item Share of net income/(loss) of associates. Starting December 2, 2019, due to the loss of significant influence in Karuna on such date, the Company is accounting for the investment in Karuna as an investment held at fair value. See Note 5 for further detail on the Group's investment in Karuna.

The following table summarizes the activity related to the investment in associates balance for the years ended December 31, 2021, 2020 and 2019.

Investment in Associates	$000's
As of January 1, 2019	—
Reclassification of Karuna investment at initial public offering	118,006
Investment in Gelesis upon deconsolidation	16,444
Share of net loss of Karuna accounted for using the equity method	(6,345)
Share of net profit of Gelesis accounted for using the equity method	37,136
Impairment of investment in Gelesis	(42,938)
Reclassification of investment upon loss of significant influence	(111,661)
As of December 31, 2019 and January 1, 2020	10,642
Share of net loss in Gelesis	(34,117)
Share of other comprehensive income in Gelesis	469
Share of losses recorded against long term interests	23,006
As of December 31, 2020 and January 1, 2021	—
Share of net loss in Gelesis	(73,703)
Share of losses recorded against long term interests	73,703
As of December 31, 2021	—

6. Investments in Associates — continued

Summarized financial information

The following table summarizes the financial information of Gelesis as included in its own financial statements, adjusted for fair value adjustments at deconsolidation and differences in accounting policies. The table also reconciles the summarized financial information to the carrying amount of the Company's interest in Gelesis. The information for the year ended December 31, 2019, includes the results of Gelesis only for the period July 1, 2019 to December 31, 2019, as Gelesis was consolidated prior to this period.

As of and for the year ended December 31,	**2021 $000s**	2020 $000s
Percentage ownership interest	**42.0%**	47.9%
Non-current assets	**357,508**	372,184
Current assets	**66,092**	92,875
Non-current liabilities	**(120,786)**	(133,743)
Current liabilities	**(537,432)**	(300,748)
Non controlling interests and options issued to third parties	**(14,216)**	(6,577)
Net assets attributable to shareholders of Gelesis Inc.	**(248,834)**	23,989
Group's share of net assets	**(104,527)**	11,481
Goodwill	**7,211**	8,216
Impairment provision balance	**(37,495)**	(42,702)
Equity method losses recorded against Long-term Interests	**96,709**	23,006
Unrecognized equity method losses (*)	**38,101**	—
Investment in associate	**—**	—

	2021 $000s	2020 $000s	2019 $000s
Revenue	**11,185**	21,442	—
Income/(loss) from continuing operations (100%)	**(271,430)**	(71,157)	74,573
Total comprehensive income/(loss) (100%)	**(273,005)**	(70,178)	74,573
Group's share in net income (losses) – limited to net investment amount	**(73,703)**	(34,117)	37,136
Group's share of total comprehensive income (loss) – limited to net investment amount	**(73,703)**	(33,648)	37,136

(*) Unrecognized equity method losses includes unrecognized other comprehensive loss of $0.7 million.

See Note 26, for the completion of the business combination of Gelesis with Capstar Special Purpose Acquisition Corp ("Capstar") on January 13, 2022. The publicly traded company began trading on the New York Stock exchange under the ticker symbol "GLS" on January 14, 2022.

On December 30, 2021, PureTech signed a Backstop agreement with Capstar according to which PureTech committed to acquire Capstar class A common shares immediately prior to the closing of the business combination between Gelesis and Capstar, in case subsequent to the redemptions of Capstar shares being completed, the Available Funds, as defined in the agreement, are less than$15.0 million. Puretech committed to acquire two thirds of the necessary shares at $10 per share so that the Available Funds increase to $15.0 million. According to the Backstop agreement, in case PureTech is required to acquire any shares under the agreement, PureTech will receive an additional 1,322,500 class A common shares of Capstar (immediately prior to the closing of the business combination) at no additional consideration.

The Company determined that such agreement meets the definition of a derivative under IFRS 9 and as such should be recorded at fair value with changes in fair value recorded through profit and loss. For the year ended December 31, 2021 the changes in fair value were de minimis. The derivative was initially recorded at fair value adjusted to defer the day 1 gain equal to the difference between the fair value of $11.2 million and transaction price of zero on the effective date and as such was initially recorded at zero. The deferred gain is amortized to Other income (expense) in the Consolidated Statement of Income (loss) over the period from the effective date until settlement date. As such, the Group recognized $0.8 million income in 2021 for the portion of the deferred gain amortized in 2021.

On January 13, 2022, as part of the conclusion of the aforementioned Backstop agreement, the Group acquired 496,145 class A common shares of Capstar for $5.0 million and received an additional 1,322,500 common A shares of Capstar for no additional consideration.

7. Operating Expenses

Total operating expenses were as follows:

For the years ending December 31,	**2021 $000s**	2020 $000s	2019 $000s
General and administrative	**57,199**	49,440	59,358
Research and development	**110,471**	81,859	85,848
Total operating expenses	**167,671**	131,299	145,206

The average number of persons employed by the Group during the year, analyzed by category, was as follows:

For the years ending December 31,	**2021**	2020	2019
General and administrative	**52**	43	39
Research and development	**119**	95	90
Total	**171**	138	129

The aggregate payroll costs of these persons were as follows:

For the years ending December 31,	**2021 $000s**	2020 $000s	2019 $000s
General and administrative	**26,438**	22,943	24,468
Research and development	**28,950**	20,674	20,682
Total	**55,388**	43,616	45,150

Detailed operating expenses were as follows:

For the years ending December 31,	**2021 $000s**	2020 $000s	2019 $000s
Salaries and wages	**36,792**	29,403	27,703
Healthcare benefits	**2,563**	1,866	1,511
Payroll taxes	**2,084**	1,629	1,468
Share-based payments	**13,950**	10,718	14,468
Total payroll costs	**55,388**	43,616	45,150
Other selling, general and administrative expenses	**30,761**	26,497	34,890
Other research and development expenses	**81,521**	61,186	65,166
Total other operating expenses	**112,282**	87,683	100,056
Total operating expenses	**167,671**	131,299	145,206

Auditor's remuneration:

For the years ending December 31,	**2021 $000s**	2020 $000s	2019 $000s
Audit of these financial statements	**1,183**	1,145	870
Audit of the financial statements of subsidiaries	**312**	291	290
Audit of the financial statements of associate**	**571**	350	—
Audit-related assurance services*	**1,868**	490	163
Non-audit related services	**—**	173	778
Total	**3,934**	2,449	2,101

* 2021 – $468.2 thousand represents prepaid expenses related to an expected initial public offering of a subsidiary.

** Audit fees of $500.0 thousand and $350.0 thousand in respect of financial statements of associates for the years ended December 31, 2021, and 2020, respectively, are not included within the consolidated financial statements. Fees related to the audit of the financial statements of associates have been disclosed in respect of both 2021 and 2020 as these fees went towards supporting the audit opinion on the Group accounts. Such amounts were not previously disclosed in the 2020 financial statements.

Please refer to Note 8 for further disclosures related to share-based payments and Note 24 for management's remuneration disclosures.

8. Share-based Payments

Share-based payments includes stock options, restricted stock units ("RSUs") and performance-based RSUs in which the expense is recognized based on the grant date fair value of these awards, except for performance based RSUs to executives that are treated as liability awards where expense is recognized based on reporting date fair value up until settlement date.

Share-based Payment Expense

The Group share-based payment expense for the years ended December 31, 2021, 2020 and 2019, were comprised of charges related to the PureTech Health plc incentive stock and stock option issuances and subsidiary stock plans.

The following table provides the classification of the Group's consolidated share-based payment expense as reflected in the Consolidated Statement of Income/(Loss):

Year ended December 31,	**2021 $000s**	2020 $000s	2019 $000s
General and administrative	**9,310**	7,650	10,677
Research and development	**4,640**	3,068	3,791
Total	**13,950**	10,718	14,468

8. Share-based Payments — continued

Ariya Stock Option Exchange- 2019

In conjunction with the acquisition of the remaining minority interests of PureTech LYT (previously named Ariya Therapeutics, Inc.) on October 1, 2019 (Please refer to Note 18), PureTech Health exchanged subsidiary stock options previously granted to the co-inventors, advisors and employees of PureTech LYT with stock options to purchase 2,147,965 of the Company's ordinary shares under the PureTech Health Performance Share Plan. As this was an exchange of awards within the consolidated group, whereby the Company's stock options were replacing Ariya's stock options, the exchange was accounted for as a modification of the original award and the incremental fair value on the date of the replacement was amortized over the remaining vesting period of the awards.

The Performance Share Plan

In June 2015, the Group adopted the Performance Stock Plan ("PSP"). Under the PSP and subsequent amendments, awards of ordinary shares may be made to the Directors, senior managers and employees of, and other individuals providing services to the Company and its subsidiaries up to a maximum authorized amount of 10.0 percent of the total ordinary shares outstanding. The shares have various vesting terms over a period of service between two and four years, provided the recipient remains continuously engaged as a service provider.

The share-based awards granted under the PSP are generally equity settled (see cash settlements below) and expire 10 years from the grant date. As of December 31, 2021, the Company had issued share-based awards to purchase an aggregate of 21,756,187 shares under this plan.

RSUs

RSU activity for the years ended December 31, 2021, 2020 and 2019 is detailed as follows:

	Number of Shares/Units	Wtd Avg Grant Date Fair Value (GBP) (*)
Outstanding (Non-vested) at January 1, 2019	**6,598,783**	**1.29**
RSUs Granted in Period	1,775,569	2.95
Vested	(3,738,005)	1.10
Forfeited	—	—
Outstanding (Non-vested) at December 31, 2019 and January 1, 2020	**4,636,347**	**2.08**
RSUs Granted in Period	1,759,011	1.80
Vested	(2,781,687)	1.54
Forfeited	(191,089)	2.37
Outstanding (Non-vested) at December 31, 2020 and January 1, 2021	**3,422,582**	**2.46**
RSUs Granted in Period	2,195,133	2.15
Vested	(1,176,695)	2.93
Forfeited	(808,305)	2.25
Outstanding (Non-vested) at December 31, 2021	**3,632,715**	**1.91**

(*) 2021 – for liability awards based on fair value at reporting date.

Each RSU entitles the holder to one ordinary share on vesting and the RSU awards are generally based on a cliff vesting schedule over a one to three-year requisite service period in which the Company recognizes compensation expense for the RSUs. Following vesting, each recipient will be required to make a payment of one pence per ordinary share on settlement of the RSUs. Vesting of the majority of the RSUs is subject to the satisfaction of performance and market conditions. The grant date fair value of market condition awards that are treated as equity settled awards is measured to reflect such conditions and there is no true-up for differences between expected and actual outcomes. For liability settled awards, see below.

The Company recognizes the estimated fair value of performance-based awards as share-based compensation expense over the performance period based upon its determination of whether it is probable that the performance targets will be achieved. The Company assesses the probability of achieving the performance targets at each reporting period. Cumulative adjustments, if any, are recorded to reflect subsequent changes in the estimated outcome of performance-related conditions.

The fair value of the market and performance-based awards is based on the Monte Carlo simulation analysis utilizing a Geometric Brownian Motion process with 100,000 simulations to value those shares. The model considers share price volatility, risk-free rate and other covariance of comparable public companies and other market data to predict distribution of relative share performance.

The performance and market conditions attached to the RSU awards are based on the achievement of total shareholder return ("TSR"), based on the achievement of absolute TSR targets, and to a lesser extent based on TSR as compared to the FTSE 250 Index, and the MSCI Europe Health Care Index. The remaining portion is based on the achievement of strategic targets. The RSU award performance criteria have changed over time as the criteria is continually evaluated by the Group's Remuneration Committee.

8. Share-based Payments — continued

In 2017, the Company granted certain executives RSUs that vested based on the service, market and performance conditions, as described above. The vesting of all RSUs was achieved by December 31, 2019 where all service, market and performance conditions were met. The remuneration committee of PureTech's Board of Directors approved the achievement of the vesting conditions as of December 31, 2019 and reached the decision during the year ended December 31, 2020 to cash settle the 2017 RSUs. The settlement value was determined based on the 3 day average closing price of the shares. The settlement value was $12.5 million (which after deducting tax withheld on behalf of recipients amounted to $7.2 million). The settlement value did not exceed the fair value at settlement date and as such the cash settlement was treated as an equity transaction in the financial statements as of and for the year ended December 31, 2020, whereby the full repurchase cash settlement amount was charged to equity in Other reserves.

Similarly in 2018, the Company granted certain executives RSUs that vested based on service, market and performance conditions, as described above. The vesting of all RSUs was achieved by December 31, 2020 where all service, market and performance conditions were met. In February 2021 the remuneration committee of PureTech's board of directors approved the achievement of the vesting conditions as of December 31, 2020 and on May 28, 2021 reached the decision to cash settle RSUs to certain employees while others were issued shares. The settlement value was determined based on the three day average closing price of the shares. The settlement value was $10.7 million (which after deducting tax withheld on behalf of recipients amounted to $6.4 million). The settlement value did not exceed the fair value at settlement date and as such the cash settlement was treated as an equity transaction, whereby the full repurchase cash settlement amount was charged to equity in Other reserves in the financial statements as of and for the year ended December 31, 2021.

Following the different cash settlements, the Company concluded that although the remaining RSUs are to be settled by shares according to their respective agreements, and any cash settlement is at the Company's discretion, due to past practice of cash settlement to multiple employees, some for multiple years, these RSUs to the company executives should be treated as liability awards and as such adjusted to fair value at every reporting date with changes in fair value recorded in earnings as stock based compensation expense.

Consequently, the Company reclassified $1.9 million from equity to other non-current liabilities and $4.8 million from equity to other payables equal to the fair value of the awards at the date of reclassification. The Company treated the excess of the fair value at the reclassification date over the grant date fair value of the RSUs (for the portion of the vesting period that has already elapsed) in the amount of $2.9 million as an equity transaction. Therefore the full amount of the liability at reclassification was recorded as a charge to equity. The changes in fair value of the liability from reclassification date to balance sheet date or settlement date are recorded as stock-based compensation expense in the Consolidated Statement of Comprehensive Income (loss).

The Company incurred share-based payment expenses for performance, market and service based RSUs of $1.5 million (including $0.6 million expense in respect of RSU liability awards), $5.7 million and $2.2 million for the years ended December 31, 2021, 2020 and 2019, respectively. The decrease in the share based compensation expense in respect of the RSUs for the year ended December 31, 2021, as compared to the year ended December 31, 2020 is due to reduction in the fair value of the liability awards as compared to their value at the date the awards were reclassified from equity awards to liability awards, as well as forfeitures of certain awards due to unexpected terminations of RSU holders.

As of December 31, 2021, the carrying amount of the RSU liability awards was $7.4 million ($4.7 million current; $2.7 million non current), out of which $4.6 million related to awards that have met all their performance and market conditions.

Stock Options

Stock option activity for the years ended December 31, 2021, 2020 and 2019, is detailed as follows:

	Number of Options	Wtd Average Exercise Price (GBP)	Wtd Average of remaining contractual term (in years)	Wtd Average Stock Price at Exercise (GBP)
Outstanding at January 1, 2019	**5,075,734**	**1.40**	**8.78**	
Granted	3,634,183	0.84		
Exercised	(237,090)	1.98		2.81
Forfeited	—	—		
Options Exercisable at December 31, 2019 and January 1, 2020	**4,349,921**	**0.93**	**8.34**	
Outstanding at December 31, 2019 and January 1, 2020	**8,472,827**	**1.16**	**8.55**	
Granted	4,076,982	3.14		
Exercised	(514,410)	1.52		2.88
Forfeited	(1,119,313)	1.88		
Options Exercisable at December 31, 2020 and January 1, 2021	**5,447,405**	**0.98**	**7.46**	
Outstanding at December 31, 2020 and January 1, 2021	**10,916,086**	**1.81**	**8.38**	
Granted	5,424,000	3.34		
Exercised	(2,238,187)	0.70		3.63
Forfeited	(687,781)	2.53		
Options Exercisable at December 31, 2021	**4,773,873**	**1.42**	**6.50**	
Outstanding at December 31, 2021	**13,414,118**	**2.58**	**8.29**	

8. Share-based Payments — continued

The fair value of the stock options awarded by the Company was estimated at the grant date using the Black-Scholes option valuation model, considering the terms and conditions upon which options were granted, with the following weighted-average assumptions:

At December 31,	**2021**	2020	2019
Expected volatility	**41.05%**	41.25%	35.68%
Expected terms (in years)	**6.16**	6.11	5.81
Risk-free interest rate	**1.06%**	0.53%	1.85%
Expected dividend yield	**—**	—	—
Grant date fair value	**$1.87**	$1.72	$2.23

The Company incurred share-based payment expense for the stock options of $6.2 million, $2.1 million and $9.2 million for the years ended December 31, 2021, 2020 and 2019, respectively. The increase in expense for the year ended December 31, 2021, as compared to the year ended December 31, 2020, is due to the new grants granted in 2021. The significant decrease for the year ended December 31, 2020, as compared to the year ended December 31, 2019, is largely attributable to the exchange of the Ariya awards with the Company's stock options in the year ended December 31, 2019, which resulted in an additional expense recorded in such year, as described above.

For shares outstanding as of December 31, 2021, the range of exercise prices is detailed as follow:

Range of Exercise Prices (GBP)	Options Outstanding	Wtd Average Exercise Price (GBP)	Wtd Average of remaining contractual term (in years)
0.01	842,762	—	7.76
1.00 to 2.00	3,521,839	1.42	5.81
2.00 to 3.00	1,251,017	2.47	8.35
3.00 to 4.00	7,798,500	3.39	9.46
Total	**13,414,118**	**2.58**	**8.29**

Subsidiary Plans

Certain subsidiaries of the Group have adopted stock option plans. A summary of stock option activity by number of shares in these subsidiaries is presented in the following table:

	Outstanding as of January 1, 2021	**Granted During the Year**	**Exercised During the Year**	**Expired During the Year**	**Forfeited During the Year**	**Outstanding as of December 31, 2021**
Alivio	**3,888,168**	**197,398**	**(2,373,750)**	**(506,260)**	**(1,205,556)**	**—**
Entrega	**962,000**	**—**	**(525,000)**	**(87,500)**	**—**	**349,500**
Follica	**1,309,040**	**1,383,080**	**—**	**(6,000)**	**—**	**2,686,120**
Sonde	**2,192,834**	**—**	**—**	**(51,507)**	**(92,323)**	**2,049,004**
Vedanta	**1,741,888**	**451,532**	**(52,938)**	**(76,491)**	**(72,354)**	**1,991,637**

	Outstanding as of January 1, 2020	Granted During the Year	Exercised During the Year	Expired During the Year	Forfeited During the Year	Outstanding as of December 31, 2020
Alivio	3,698,244	189,924	—	—	—	3,888,168
Entrega	972,000	—	—	—	(10,000)	962,000
Follica	1,309,040	—	—	—	—	1,309,040
Sonde	1,829,004	363,830	—	—	—	2,192,834
Vedanta	1,450,100	493,951	(813)	—	(201,350)	1,741,888

8. Share-based Payments — continued

	Outstanding as of January 1, 2019	Granted During the Year	Exercised During the Year	Expired During the Year	Forfeited During the Year	Outstanding as of December 31, 2019
Gelesis	3,681,732	—	—	(110,386)	(3,571,346)[1]	—
Alivio	2,393,750	1,329,494	(3,125)	—	(21,875)	3,698,244
PureTech LYT	2,180,000	—	—	—	(2,180,000)[2]	—
Commense	540,416	—	—	—	(540,416)	—
Entrega	914,000	58,000	—	—	—	972,000
Follica	1,229,452	79,588	—	—	—	1,309,040
Karuna	1,949,927	—	—	—	(1,949,927)[1]	—
Sonde	22,500	1,806,504	—	—	—	1,829,004
Vedanta	1,373,750	154,193	—	—	(77,843)	1,450,100

1 These shares represent the options outstanding on the date of deconsolidation of Karuna and Gelesis.
2 These shares represent the options outstanding on the date of exchange to PureTech stock options.

The weighted-average exercise prices and remaining contractual life for the options outstanding as of December 31, 2021, were as follows:

Outstanding at December 31, 2021	**Number of options**	**Weighted-average exercise price $**	**Weighted-average contractual life outstanding**
Alivio	**—**	**—**	**0**
Entrega	**349,500**	**1.88**	**4.62**
Follica	**2,686,120**	**1.39**	**7.28**
Sonde	**2,049,004**	**0.20**	**7.71**
Vedanta	**1,991,637**	**13.42**	**5.92**

The weighted average exercise prices for the options granted for the years ended December 31, 2021, 2020 and 2019, were as follows:

For the years ended December 31,	**2021 $**	2020 $	2019 $
Alivio	**—**	0.47	0.49
Follica	**1.86**	—	0.03
Sonde	**—**	0.18	0.20
Vedanta	**19.69**	19.59	19.13

The weighted average exercise prices for options forfeited during the year ended December 31, 2021, were as follows:

Forfeited during the year ended December 31, 2021	**Number of options**	**Weighted-average exercise price $**
Alivio	**1,205,556**	**0.48**
Sonde	**92,323**	**0.18**
Vedanta	**72,354**	**19.36**

The weighted average exercise prices for options exercised during the year ended December 31, 2021, were as follows:

Exercised during the year ended December 31, 2021	**Number of options**	**Weighted-average exercise price $**
Alivio	**2,373,750**	**0.03**
Entrega	**525,000**	**0.03**
Vedanta	**52,938**	**0.96**

8. Share-based Payments — continued

The weighted average exercise prices for options exercisable as of December 31, 2021, were as follows:

Exercisable at December 31, 2021	Number of Options	Weighted-average exercise price $	Exercise Price Range $
Alivio	—	—	—
Entrega	**349,500**	**1.88**	**0.03-2.36**
Follica	**2,686,120**	**1.01**	**0.03-1.86**
Sonde	**2,049,004**	**0.20**	**0.13-0.20**
Vedanta	**1,991,637**	**9.64**	**0.02-19.94**

Significant Subsidiary Plans

Vedanta 2010 Stock Incentive Plan

In 2010, the Board of Directors for Vedanta approved the 2010 Stock Incentive Plan (the "Vedanta Plan"). Through subsequent amendments, as of December 31, 2021, it allowed for the issuance of 2,797,055 share-based compensation awards through incentive share options, nonqualified share options, and restricted shares to employees, Directors, and nonemployees providing services to Vedanta. At December 31, 2021, 747,270 shares remained available for issuance under the Vedanta Plan.

The options granted under Vedanta Plan are equity settled and expire 10 years from the grant date. Typically, the awards vest in four years but vesting conditions can vary based on the discretion of Vedanta's Board of Directors.

Options granted under the Vedanta Plan are exercisable at a price per share not less than the fair market value of the underlying ordinary shares on the date of grant. The estimated fair value of options, including the effect of estimated forfeitures, is recognized over the options' vesting period.

The fair value of the stock option grants has been estimated at the date of grant using the Black-Scholes option pricing model with the following range of assumptions:

Assumption/Input	**2021**	2020	2019
Expected award life (in years)	**6.00-7.11**	6.00-10.00	5.86-6.07
Expected award price volatility	**88.05%-88.59%**	89.24%-95.46%	89.24%-95.46%
Risk free interest rate	**0.96%-1.32%**	0.32%-0.87%	1.73%-1.88%
Expected dividend yield	**—**	—	—
Grant date fair value	**$13.84-$16.23**	$13.09-$16.54	$14.12-$15.61
Share price at grant date	**$19.00-$21.35**	$19.59	$18.71-$19.94

Vedanta incurred share-based compensation expense of $5.4 million, $2.4 million and $1.7 million for the years ended December 31, 2021, 2020 and 2019, respectively.

Other Plans

The stock compensation expense under plans at other subsidiaries of the Group not including Vedanta amounted to $0.84 million, $0.42 million and $0.01 million for the years ended December 31, 2021, 2020 and 2019, respectively.

9. Finance Cost, net

The following table shows the breakdown of finance income and costs:

For the years ended December 31,	**2021 $000s**	2020 $000s	2019 $000s
Finance income			
Interest income from financial assets	**214**	1,183	4,362
Total finance income	**214**	1,183	4,362
Finance costs			
Contractual interest expense on notes payable	**(1,031)**	(96)	(149)
Interest expense on other borrowings	**(1,502)**	(496)	—
Interest expense on lease liability	**(2,181)**	(2,354)	(2,495)
Gain/(loss) on foreign currency exchange	**(56)**	—	68
Total finance cost – contractual	**(4,771)**	(2,946)	(2,576)
Gain/(loss) from change in fair value of warrant liability	**1,419**	(117)	(11,890)
Gain/(loss) from change in fair value of preferred shares	**8,362**	(4,234)	(34,585)
Gain/(loss) from change in fair value of convertible debt	**(175)**	—	—
Total finance income/(costs) – fair value accounting	**9,606**	(4,351)	(46,475)
Total finance costs – subsidiary preferred shares	**—**	—	(1,458)
Total finance income/(costs)	**9,606**	(4,351)	(47,933)
Finance income/(costs), net	**5,050**	(6,115)	(46,147)

10. Earnings/(Loss) per Share

The basic and diluted loss per share has been calculated by dividing the income/(loss) for the period attributable to ordinary shareholders by the weighted average number of ordinary shares outstanding during the years ended December 31, 2021, 2020 and 2019, respectively. During the year ended December 31, 2021 the Company incurred a net loss and therefore all outstanding potential securities were considered anti-dilutive. The amount of potential securities that were excluded from the calculation amounted to 6,553,905 shares.

Earnings/(Loss) Attributable to Owners of the Company:

	2021		2020		2019	
	Basic $000s	**Diluted $000s**	Basic $000s	Diluted $000s	Basic $000s	Diluted $000s
Income/(loss) for the year, attributable to the owners of the Company	**(60,558)**	**(60,558)**	5,985	5,985	421,144	421,144
Income/(loss) attributable to ordinary shareholders	**(60,558)**	**(60,558)**	5,985	5,985	421,144	421,144

Weighted-Average Number of Ordinary Shares:

	2021		2020		2019	
	Basic	**Diluted**	Basic	Diluted	Basic	Diluted
Issued ordinary shares at January 1,	**285,885,025**	**285,885,025**	285,370,619	285,370,619	282,493,867	282,493,867
Effect of shares issued	**705,958**	**705,958**	233,048	233,048	932,600	932,600
Effect of dilutive shares (please refer to Note 8)	**—**	**—**	—	7,252,246	—	8,355,866
Weighted average number of ordinary shareholders at December 31,	**286,590,983**	**286,590,983**	285,603,667	292,855,913	283,426,467	291,782,333

Earnings/(Loss) per Share:

	2021		2020		2019	
	Basic $	**Diluted $**	Basic $	Diluted $	Basic $	Diluted $
Basic and diluted earnings/(loss) per share	**(0.21)**	**(0.21)**	0.02	0.02	1.49	1.44

11. Property and Equipment

Cost	Laboratory and Manufacturing Equipment $000s	Furniture and Fixtures $000s	Computer Equipment and Software $000s	Leasehold Improvements $000s	Construction in process $000s	Total $000s
Balance as of January 1, 2020	7,385	1,452	1,508	17,656	646	28,647
Additions, net of transfers	1,536	—	51	399	3,347	5,332
Disposals	(642)	—	(40)	—	—	(682)
Reclassifications	141	—	—	—	(141)	—
Balance as of December 31, 2020	8,420	1,452	1,519	18,054	3,852	33,297
Additions, net of transfers	1,424	—	92	183	6,723	8,422
Disposals	(323)	—	(282)	—	—	(605)
Reclassifications	2,211	—	—	248	(2,459)	—
Balance as of December 31, 2021	**11,733**	**1,452**	**1,329**	**18,485**	**8,116**	**41,115**

Accumulated depreciation and impairment loss	Laboratory and Manufacturing Equipment $000s	Furniture and Fixtures $000s	Computer Equipment and Software $000s	Leasehold Improvements $000s	Construction in process $000s	Total $000s
Balance as of January 1, 2020	(2,968)	(239)	(1,030)	(2,955)	—	(7,192)
Depreciation	(1,572)	(215)	(297)	(1,860)	—	(3,944)
Disposals	576	—	40	—	—	616
Balance as of December 31, 2020	(3,965)	(454)	(1,287)	(4,815)	—	(10,520)
Depreciation	(1,973)	(208)	(174)	(1,991)	—	(4,346)
Disposals	251	—	271	—	—	522
Balance as of December 31, 2021	**(5,686)**	**(663)**	**(1,190)**	**(6,806)**	**—**	**(14,344)**

Property and Equipment, net	Laboratory and Manufacturing Equipment $000s	Furniture and Fixtures $000s	Computer Equipment and Software $000s	Leasehold Improvements $000s	Construction in process $000s	Total $000s
Balance as of December 31, 2020	4,456	998	232	13,239	3,852	22,777
Balance as of December 31, 2021	**6,047**	**790**	**139**	**11,679**	**8,116**	**26,771**

Depreciation of property and equipment is included in the General and administrative expenses and Research and development expenses line items in the Consolidated Statements of Comprehensive Income/(Loss). The Company recorded depreciation expense of $4.3 million, $3.9 million and $3.2 million for the years ended December 31, 2021, 2020 and 2019, respectively.

12. Intangible Assets

Intangible assets consist of licenses of intellectual property acquired by the Group through various agreements with third parties and are recorded at the value of the consideration transferred. Information regarding the cost and accumulated amortization of intangible assets is as follows:

Cost	Licenses $000s
Balance as of January 1, 2020	625
Additions	275
Balance as of December 31, 2020	900
Additions	90
Balance as of December 31, 2021	**990**

Accumulated amortization	Licenses $000s
Balance as of January 1, 2020	—
Amortization	(1)
Balance as of December 31, 2020	(1)
Amortization	(2)
Balance as of December 31, 2021	**(3)**

Intangible assets, net	Licenses $000s
Balance as of December 31, 2020	899
Balance as of December 31, 2021	**987**

Substantially all the intangible asset licenses represent in-process-research-and-development assets since they are still being developed and are not ready for their intended use. As such, these assets are not yet amortized but tested for impairment annually.

The Company tested such assets for impairment as of balance sheet date and concluded that none were impaired.

Amortization expense was included in the Research and development expenses line item in the accompanying Consolidated Statements of Comprehensive Income/(Loss). Amortization expense, recorded using the straight-line method, was approximately $0.0 million, $0.0 million and $0.1 million for the years ended December 31, 2021 2020 and 2019, respectively.

13. Other Financial Assets

Other financial assets consist of restricted cash held, which represents amounts that are reserved as collateral against letters of credit with a bank that are issued for the benefit of a landlord in lieu of a security deposit for office space leased by the Group. Information regarding restricted cash was as follows:

As of December 31,	**2021 $000s**	2020 $000s
Restricted cash	**2,124**	2,124
Total other financial assets	**2,124**	2,124

14. Equity

Total equity for PureTech as of December 31, 2021, and 2020, was as follows:

Equity	**December 31, 2021 $000s**	December 31, 2020 $000s
Share capital, £0.01 par value, issued and paid 287,796,585 and 285,885,025 as of December 31, 2021 and 2020, respectively	**5,444**	5,417
Merger Reserve	**138,506**	138,506
Share premium	**289,303**	288,978
Translation reserve	**469**	469
Other reserves	**(40,077)**	(24,050)
Retained earnings/(accumulated deficit)	**199,871**	260,429
Equity attributable to owners of the Group	**593,515**	669,748
Non-controlling interests	**(9,368)**	(16,209)
Total equity	**584,147**	653,539

Changes in share capital and share premium relate primarily to incentive options exercises during the period.

Shareholders are entitled to vote on all matters submitted to shareholders for a vote. Each ordinary share is entitled to one vote. Each ordinary share is entitled to receive dividends when and if declared by the Company's Directors. The Company has not declared any dividends in the past.

On June 18, 2015, the Company acquired the entire issued share capital of PureTech LLC in return for 159,648,387 Ordinary Shares. This was accounted for as a common control transaction at cost. It was deemed that the share capital was issued in line with movements in share capital as shown prior to the transaction taking place. In addition, the merger reserve records amounts previously recorded as share premium.

Other reserves comprise the cumulative credit to share-based payment reserves corresponding to share-based payment expenses recognized through Consolidated Statements of Comprehensive Income/(Loss), settlements of vested share based payment awards as well as other additions that flow directly through equity such as the excess or deficit from changes in ownership of subsidiaries while control is maintained by the Group.

15. Subsidiary Preferred Shares

Preferred shares issued by subsidiaries and affiliates often contain redemption and conversion features that are assessed under IFRS 9 in conjunction with the host preferred share instrument. This balance represents subsidiary preferred shares issued to third parties.

The subsidiary preferred shares are redeemable upon the occurrence of a contingent event, other than full liquidation of the Company, that is not considered to be within the control of the Company. Therefore these subsidiary preferred shares are classified as liabilities. These liabilities are measured at fair value through profit and loss. The preferred shares are convertible into ordinary shares of the subsidiaries at the option of the holder and mandatorily convertible into ordinary shares upon a subsidiary listing in a public market at a price above that specified in the subsidiary's charter or upon the vote of the holders of subsidiary preferred shares specified in the charter. Under certain scenarios the number of ordinary shares receivable on conversion will change and therefore, the number of shares that will be issued is not fixed. As such the conversion feature is considered to be an embedded derivative that normally would require bifurcation. However, since the preferred share liabilities are measured at fair value through profit and loss, as mentioned above, no bifurcation is required.

The preferred shares are entitled to vote with holders of common shares on an as converted basis.

The Group recognized the preferred share balance upon the receipt of cash financing or upon the conversion of notes into preferred shares at the amount received or carrying balance of any notes and derivatives converted into preferred shares.

The balance as of December 31, 2021 and 2020, represents the fair value of the instruments for all subsidiary preferred shares. The following summarizes the subsidiary preferred share balance:

As of December 31,	**2021 $000s**	2020 $000s
Entrega	**669**	1,291
Follica	**11,191**	12,792
Sonde	**13,362**	12,821
Vedanta Biosciences	**148,796**	92,068
Total subsidiary preferred share balance	**174,017**	118,972

15. Subsidiary Preferred Shares — continued

As is customary, in the event of any voluntary or involuntary liquidation, dissolution or winding up of a subsidiary, the holders of subsidiary preferred shares which are outstanding shall be entitled to be paid out of the assets of the subsidiary available for distribution to shareholders and before any payment shall be made to holders of ordinary shares. A merger, acquisition, sale of voting control or other transaction of a subsidiary in which the shareholders of the subsidiary immediately before the transaction do not own a majority of the outstanding shares of the surviving company shall be deemed to be a liquidation event. Additionally, a sale, lease, transfer or other disposition of all or substantially all of the assets of the subsidiary shall also be deemed a liquidation event.

As of December 31, 2021 and 2020, the minimum liquidation preference reflects the amounts that would be payable to the subsidiary preferred holders upon a liquidation event of the subsidiaries, which is as follows:

As of December 31,	**2021 $000s**	2020 $000s
Entrega	**2,216**	2,216
Follica	**6,405**	6,405
Sonde	**12,000**	12,000
Vedanta Biosciences	**149,568**	86,161
Total minimum liquidation preference	**170,189**	106,782

For the years ended December 31, 2021 and 2020, the Group recognized the following changes in the value of subsidiary preferred shares:

	$000s
Balance as of January 1, 2020	100,989
Issuance of new preferred shares	13,750
Increase in value of preferred shares measured at fair value	4,234
Balance as of January 1, 2021	118,972
Issuance of new preferred shares - financing cash flow	37,610
Conversion of convertible notes into preferred shares - non cash financing activity	25,797
decrease in value of preferred shares measured at fair value - finance costs (income)	(8,362)
Balance as December 31, 2021	**174,017**

2021

On July 21, 2021 Vedanta closed a Series D financing in which Vedanta issued 2,387,675 Preferred D shares for consideration of $68.4 million. From such consideration of $68.4 million, $25.8 million was received from Pfizer through conversion of its convertible note (see Note 17) and $5.0 million was received from PureTech in exchange for 174,520 Preferred D shares. The amount received from PureTech was eliminated in the consolidated financial statements.

2020

In January 2020 and April 2020, Sonde Health issued and sold shares of Series A-2 preferred shares for aggregate proceeds of $4.8 million, of which none was contributed by PureTech.

In April 2020 and July 2020, Vedanta issued and sold shares of Series C-2 preferred shares for aggregate proceeds of $9.0 million, of which none was contributed by PureTech.

16. Financial Instruments

The Group's financial instruments consist of financial liabilities, including preferred shares, convertible notes, warrants and loans payable, as well as financial assets classified as assets held at fair value.

Fair Value Process

For financial instruments measured at fair value under IFRS 9 the change in the fair value is reflected through profit and loss. Using the guidance in IFRS 13, the total business enterprise value and allocable equity of each entity being valued was determined using a discounted cash flow income approach, replacement cost/asset approach, market/asset – PWERM approach, or market backsolve approach through a recent arm's length financing round. The approaches, in order of strongest fair value evidence, are detailed as follows:

Valuation Method	Description
Market – Backsolve	The market backsolve approach benchmarks the original issue price (OIP) of the company's latest funding transaction as current value.
Market/Asset – PWERM	Under a PWERM, the company value is based upon the probability-weighted present value of expected future investment returns, considering each of the possible future outcomes available to the enterprise. An Asset approach may be included as an expected future outcome within the PWERM method. Possible future outcomes can include IPO scenarios, potential SPAC transactions, merger and acquisition transactions as well as other similar exit transactions of the investee.
Income Based – DCF	The income approach is used to estimate fair value based on the income streams, such as cash flows or earnings, that an asset or business can be expected to generate.
Asset/Cost	The asset/cost approach considers reproduction or replacement cost as an indicator of value.

As of December 31, 2021 and 2020, at each measurement date, the total fair value of preferred shares and warrants, including embedded conversion rights that are not bifurcated, was determined using the following allocation methods: option pricing model ("OPM"), Probability-Weighted Expected Return Method ("PWERM"), or Hybrid allocation framework. The methods are detailed as follows:

Allocation Method	Description
OPM	The OPM model treats preferred stock as call options on the enterprise's equity value, with exercise prices based on the liquidation preferences of the preferred stock.
PWERM	Under a PWERM, share value is based upon the probability-weighted present value of expected future investment returns, considering each of the possible future outcomes available to the enterprise, as well as the rights of each share class.
Hybrid	The hybrid method ("HM") is a combination of the PWERM and OPM. Under the hybrid method, multiple liquidity scenarios are weighted based on the probability of the scenarios occurrence, similar to the PWERM, while also utilizing the OPM to estimate the allocation of value in one or more of the scenarios.

Valuation policies and procedures are regularly monitored by the Company's finance group. Fair value measurements, including those categorized within Level 3, are prepared and reviewed on their issuance date and then on an annual basis for reasonableness and compliance with the fair value measurements guidance under IFRS. The Group measures fair values using the following fair value hierarchy that reflects the significance of the inputs used in making the measurements:

Fair Value Hierarchy Level	Description
Level 1	Inputs that are quoted market prices (unadjusted) in active markets for identical instruments.
Level 2	Inputs other than quoted prices included within Level 1 that are observable either directly (i.e. as prices) or indirectly (i.e. derived from prices).
Level 3	Inputs that are unobservable. This category includes all instruments for which the valuation technique includes inputs not based on observable data and the unobservable inputs have a significant effect on the instrument's valuation.

Whilst the Group considers the methodologies and assumptions adopted in fair value measurements as supportable, reasonable and robust, because of the inherent uncertainty of valuation, those estimated values may differ significantly from the values that would have been used had a ready market for the investment existed.

COVID-19 Consideration

At December 31, 2021, the Group assessed certain key assumptions within the valuation of its unquoted instruments and considered the impact of the COVID-19 pandemic on all unobservable inputs (Level 3). The assumptions considered with respect to COVID-19 included but were not limited to the following: exit scenarios and timing, discount rates, revenue assumptions as well as volatilities. The Group views any impact of the COVID-19 pandemic on its unquoted instruments as immaterial as of December 31, 2021.

16. Financial Instruments — continued

Subsidiary Preferred Shares Liability and Subsidiary Convertible Notes

The following table summarizes the changes in the Group's subsidiary preferred shares and convertible note liabilities measured at fair value, which were categorized as Level 3 in the fair value hierarchy:

	Subsidiary Preferred Shares $000s	Subsidiary Convertible Notes $000s
Balance at January 1, 2019	217,519	9,333
Value at issuance	51,048	1,607
Conversion to preferred	4,894	(4,894)
Conversion to common	—	(2,418)
Deconsolidation	(207,346)	(5,017)
Change in fair value	33,636	1,389
Finance Costs	1,458	—
Other	(112)	—
Cash distribution	(108)	—
Balance at December 31, 2019 and January 1, 2020	100,989	—
Value at issuance	13,750	25,000
Change in fair value	4,234	—
Balance at December 31, 2020 and January 1, 2021	118,972	25,000
Value at issuance	37,610	2,215
Conversion to subsidiary preferred shares	25,797	(25,797)
Accrued interest – contractual	—	867
Change in fair value	(8,362)	175
Balance at December 31, 2021	**174,017**	**2,461**

The change in fair value of preferred shares and convertible notes are recorded in Finance income/(costs) – fair value accounting in the Consolidated Statements of Comprehensive Income/(Loss).

The table below sets out information about the significant unobservable inputs used at December 31, 2021, in the fair value measurement of the Group's material subsidiary preferred shares liabilities categorized as Level 3 in the fair value hierarchy:

Fair Value at December 31, 2021	Valuation Technique	Unobservable Inputs	Weighted Average	Sensitivity to Decrease in Input
148,796	Market/Asset – PWERM & Hybrid allocation	Estimated time to exit Discount rate Volatility	0.93 30.0% 95.0%	Fair value increase
11,860	Income – DCF & OPM allocation	Estimated time to exit Probability of Success	2.94 76.5%	Fair value decrease
		Discount rate	21.9%	Fair value increase
		Terminal value growth rate Volatility	(1.3)% 57.1%	Fair value decrease
13,362	Market – Backsolve & OPM allocation	Estimated time to exit Volatility	2.00 40.0%	Fair value increase

Subsidiary Preferred Shares Sensitivity

The following summarizes the sensitivity from the assumptions made by the Company with respect to the significant unobservable inputs which are categorized as Level 3 in the fair value hierarchy and used in the fair value measurement of the Group's subsidiary preferred shares liabilities (Please refer to Note 15):

Input	Subsidiary Preferred Share Liability	
As of December 31, 2021	Sensitivity Range	Financial Liability Increase/(Decrease) $000s
Subsidiary Enterprise Value	-2%	(3,041)
	+2%	3,140
Time to Liquidity	-6 Months	5,934
	+6 Months	(6,838)
Volatility	-10%	737
	+10%	(682)
Discount Rate	-5%	10,575
	+5%	(6,068)

16. Financial Instruments — continued

Subsidiary Convertible Notes

Vedanta issued convertible promissory notes in December 2020 and Sonde issued convertible notes in April 2021 and November 2021 (collectively the "Notes"). See Note 17 Subsidiary Notes payable for further details. The Notes contain one or more embedded derivatives. The Company elected to account for these Notes as FVTPL liabilities, whereby the embedded derivatives are not bifurcated but rather the Notes are recorded at fair value with changes in fair value recorded in the Finance Income (Cost) line item in the Consolidated statement of comprehensive income (loss).

In July 2021 the entire convertible note issued by Vedanta was converted into Vedanta Series D preferred shares – see Note 15 for further details.

The aggregate fair value of the Sonde Notes was determined to be approximately $2.5 million at December 31, 2021. The valuations of the Notes were each categorized as Level 3 in the fair value hierarchy. In estimating the fair value of these Notes, a probability-weighted methodology was utilized, whereby the Notes' expected returns under various Note-specific liquidity scenarios were analyzed and weighted to arrive at a probability-adjusted fair value at December 31, 2021. The significant unobservable input used at December 31, 2021, in the fair value measurement of Sonde's convertible notes constituted the estimated time to exit, which was 0.59 years.

Financial Assets Held at Fair Value

Karuna and Vor Valuation

Karuna (Nasdaq: KRTX) and Vor (Nasdaq: VOR) and additional immaterial investments are listed entities on an active exchange and as such the fair value for the year ended December 31, 2021, was calculated utilizing the quoted common share price. Please refer to Note 5 for further details.

Akili and Gelesis

In accordance with IFRS 9, the Company accounts for its preferred share investments in Akili and Gelesis as financial assets held at fair value through the profit and loss. During the year ended December 31, 2021, the Company recorded its investment in such preferred shares at fair value and recognized the change in fair value of such investments as a gain of $66.7 million that was recorded to the Consolidated Statements of Comprehensive Income/(Loss) in the line item Gain/(loss) on investments held at fair value.

The following table summarizes the changes in the Group's investments held at fair value, which were categorized as Level 3 in the fair value hierarchy:

	$'000s
Balance at January 1, 2019	85,163
Deconsolidation of Vor	12,028
Deconsolidation of Karuna	77,373
Deconsolidation of Gelesis	49,170
Reclass of Karuna to Associate	(118,006)
Gain/(Loss) on changes in fair value	48,867
Issuance of note receivable	6,480
Conversion of note receivable	(6,630)
Balance at December 31, 2019 and January 1, 2020	154,445
Cash purchase of Gelesis preferred shares (please refer to Note 6)	10,000
Cash purchase of Vor preferred shares	1,150
Gain/(Loss) on changes in fair value	41,297
Balance at January 1, 2021 before allocation of associate loss to long-term interest	206,892
Cash purchase of Vor preferred shares	500
Reclassification of Vor from level 3 to level 1	(33,365)
Gain/(Loss) on changes in fair value	65,505
Balance as of December 31, 2021 before allocation of associate loss to long-term interest	**239,533**
Share of associate loss allocated to long-term interest (please refer to Note 5)	(96,709)
Balance as of December 31, 2021 after allocation of associate loss to long-term interest	**142,824**

The change in fair value of investments held at fair value are recorded in Gain/(loss) on investments held at fair value in the Consolidated Statements of Comprehensive Income/(Loss).

The table below sets out information about the significant unobservable inputs used at December 31, 2021, in the fair value measurement of the Group's material investments held at fair value categorized as Level 3 in the fair value hierarchy:

Fair Value at December 31, 2021	Valuation Technique	Unobservable Inputs	Weighted Average	Sensitivity to Decrease in Input
238,231	Market – PWERM & Hybrid allocation	Estimated time to exit (*)	0.76	
		Discount rate	20.0%	Fair value increase
		Volatility	62.0%	

16. Financial Instruments — continued

The following summarizes the sensitivity from the assumptions made by the Company with respect to the significant unobservable inputs which are categorized as Level 3 in the fair value hierarchy and used in the fair value measurement of the Group's investments held at fair value (Please refer to Note 5):

Input	Investments Held at Fair Value	
As of December 31, 2021	Sensitivity Range	Financial Asset Increase/ (Decrease) $000s
Investee Enterprise Value	-2%	(4,559)
	+2%	4,652
Time to Liquidity (*)	-6 Months	11,828
	+6 Months	(14,691)
Discount Rate	-5%	3,842
	+5%	(3,408)

(*) Gelesis investment in preferred shares was excluded from the sensitivity calculation with regard to the time to liquidity as changing the time to liquidity in the Gelesis valuation would result in an unreasonable assumption leading to an unreasonable alternative value considering the circumstances on the financial reporting date.

Warrants

Warrants issued by subsidiaries within the Group are classified as liabilities, as they will be settled in a variable number of preferred shares. The following table summarizes the changes in the Group's subsidiary warrant liabilities, which were categorized as Level 3 in the fair value hierarchy:

	Subsidiary Warrant Liability $000s
Balance at January 1, 2019	13,012
Warrant Issuance	4,706
Gelesis Deconsolidation	(21,611)
Change in fair value	11,890
Balance at December 31, 2019 and January 1, 2020	7,997
Warrant Issuance	92
Change in fair value	117
Balance at December 31, 2020 and January 1, 2021	8,206
Change in fair value - finance costs (income)	(1,419)
Balance at December 31, 2021	**6,787**

The change in fair value of warrants are recorded in Finance income/(costs) – fair value accounting in the Consolidated Statements of Comprehensive Income/(Loss).

In connection with various amendments to its 2010 Loan and Security Agreement, Follica issued Series A-1 preferred share warrants at various dates in 2013 and 2014. Each of the warrants has an exercise price of $0.14 and a contractual term of ten years from the date of issuance. In 2017, in conjunction with the issuance of convertible notes, the exercise price of the warrants was adjusted to $0.07 per share.

In connection with the September 2, 2020 Oxford Finance LLC loan issuance, Vedanta also issued Oxford Finance LLC 12,886 Series C-2 preferred share warrants with an exercise price of $23.28 per share, expiring September 2030.

The $6.8 million warrant liability at December 31, 2021, was largely attributable to the outstanding Follica preferred share warrants.

The table below sets out the weighted average of significant unobservable inputs used at December 31, 2021, with respect to determining the fair value of the Group's warrants categorized as Level 3 in the fair value hierarchy:

Assumption/Input	Warrants
Expected term	1.66
Expected volatility	49.1%
Risk free interest rate	0.7%
Expected dividend yield	—%
Estimated fair value of the preferred share	$2.72

16. Financial Instruments — continued

The following summarizes the sensitivity from the assumptions made by the Company with respect to the significant unobservable inputs which are categorized as Level 3 in the fair value hierarchy and used in the fair value measurement of the Group's warrant liabilities:

Input	Warrant Liability	
As at December 31, 2021	Sensitivity Range	Financial Liability Increase/(Decrease) $000s
Discount Rate used in the calculation of estimated fair value of the preferred share	-5%	8,390
	+5%	(4,222)

Short-term Note from Associate

On December 7, 2021, Gelesis issued PureTech a $15.0 million note to be repaid the earlier of three business days after the closing of the business combination of Gelesis with Capstar Special Acquisition Corp ("Capstar"), or 30 days following the termination of such business combination. In the event of the business combination termination, the Company, who represented the majority of the note holders, could have elected to convert the note at the next equity financing at a discount of 25% from the financing price. The note bears interest at a rate of 10% per annum.

The note was repaid by Gelesis in January 2022 due to the closing of the business combination between Gelesis and Capstar on January 13, 2022.

The Note is measured at fair value in accordance with IFRS 9 with changes in fair value recorded as profit or loss in the Consolidated Statement of Comprehensive Income/(Loss). The fair value as of December 31, 2021, of $15.1 million approximated the note's contractual amount and the change in fair value from issuance date to December 31, 2021, was not material.

Fair Value Measurement and Classification

The fair value of financial instruments by category at December 31, 2021 and 2020:

	2021					
	Carrying Amount		**Fair Value**			
	Financial Assets $000s	**Financial Liabilities $000s**	**Level 1 $000s**	**Level 2 $000s**	**Level 3 $000s**	**Total $000s**
Financial assets:						
Money Markets[1]	**432,649**	**—**	**432,649**	**—**	**—**	**432,649**
Short-term note from associate	**15,120**	**—**	**—**	**—**	**15,120**	**15,120**
Investments held at fair value[2]	**493,888**	**—**	**254,355**	**—**	**239,533**	**493,888**
Trade and other receivables[3]	**3,174**	**—**	**—**	**3,174**	**—**	**3,174**
Total financial assets	**944,832**	**—**	**687,005**	**3,174**	**254,653**	**944,832**
Financial liabilities:						
Subsidiary warrant liability	**—**	**6,787**	**—**	**—**	**6,787**	**6,787**
Subsidiary preferred shares	**—**	**174,017**	**—**	**—**	**174,017**	**174,017**
Subsidiary notes payable	**—**	**3,916**	**—**	**1,330**	**2,586**	**3,916**
Share based liability awards	**—**	**7,362**	**6,081**	**—**	**1,281**	**7,362**
Total financial liabilities	**—**	**192,082**	**6,081**	**1,330**	**184,671**	**192,082**

1 Issued by a diverse group of corporations, largely consisting of financial institutions, virtually all of which are investment grade.
2 Balance prior to share of associate loss allocated to long-term interest (please refer to Note 5).
3 Outstanding receivables are owed primarily by government agencies, virtually all of which are investment grade.

	2020					
	Carrying Amount		Fair Value			
	Financial Assets $000s	Financial Liabilities $000s	Level 1 $000s	Level 2 $000s	Level 3 $000s	Total $000s
Financial assets:						
Money Markets[1]	394,143	—	394,143	—	—	394,143
Investments held at fair value[2]	553,167	—	346,275	—	206,892	553,167
Loans and receivables:						
Trade and other receivables[3]	2,558	—	—	2,558	—	2,558
Total financial assets	949,867	—	740,417	2,558	206,892	949,867
Financial liabilities:						
Subsidiary warrant liability	—	8,206	—	—	8,206	8,206
Subsidiary preferred shares	—	118,972	—	—	118,972	118,972
Subsidiary notes payable	—	26,455	—	1,330	25,125	26,455
Total financial liabilities	—	153,633	—	1,330	152,303	153,633

1 Issued by a diverse group of corporations, largely consisting of financial institutions, virtually all of which are investment grade.
2 Balance prior to share of associate loss allocated to long-term interest (please refer to Note 5).
3 Outstanding receivables are owed primarily by corporations and government agencies, virtually all of which are investment grade.

17. Subsidiary Notes Payable

The subsidiary notes payable are comprised of loans and convertible notes. As of December 31, 2021 and 2020, the loan in Follica and the financial instruments for Knode and Appeering did not contain embedded derivatives and therefore these instruments continue to be held at amortized cost. The notes payable consist of the following:

As of December 31,	**2021 $000s**	2020 $000s
Loans	**1,330**	1,330
Convertible notes	**2,586**	25,125
Total subsidiary notes payable	**3,916**	26,455

Loans

In October 2010, Follica entered into a loan and security agreement with Lighthouse Capital Partners VI, L.P. The loan is secured by Follica's assets, including Follica's intellectual property and bears interest at a rate of 12.0 percent. The outstanding loan balance totaled approximately $1.3 million and $1.3 million as of December 31, 2021 and December 31, 2020. The accrued interest on such loan balance is presented as Other current liabilities and totaled approximately $0.6 million and $0.5 million as of December 31, 2021 and December 31, 2020, respectively. The increase in 2021 is attributed to interest expense for the year ended December 31, 2021.

Convertible Notes

Convertible Notes outstanding were as follows:

	Vedanta $000s	Knode $000s	Appeering $000s	Sonde $000s	Total $000s
January 1, 2020	—	50	75	—	125
Gross principal – issuance of notes	25,000	—	—	—	25,000
Change in fair value	—	—	—	—	—
December 31, 2020 and January 1, 2021	25,000	50	75	—	25,125
Gross principal – issuance of notes – financing activity	—	—	—	2,215	2,215
Accrued interest on convertible notes – finance costs	797	—	—	70	867
Conversion to subsidiary preferred shares	(25,797)	—	—	—	(25,797)
Change in fair value – finance costs	—	—	—	175	175
December 31, 2021	**—**	**50**	**75**	**2,461**	**2,586**

On December 30, 2020, Vedanta issued a $25.0 million convertible promissory note to an investor. The note bore interest at an annual rate of 6.0 percent and its maturity date was the first anniversary of the note. Prepayment of the note was not allowed and there was no conversion discount feature on the note. The note was mandatorily convertible in a Qualified equity financing and a Qualified Public Offering at the current price of the financing or offering, all as defined in the note purchase agreement. In addition, the note allowed for optional conversion immediately prior to a Non Qualified public offering, Non Qualified Equity financing, or a Corporate transaction and for a pay-out in the case of a change of control transaction. On July 19, 2021, upon the occurrence of Vedanta's Series D preferred share issuance that was considered to be a Qualified Equity Financing, the entire outstanding amount of the note, principal and interest, was converted into Series D preferred shares of Vedanta at the current price of the financing. For further details, please see Note 15.

On April 6, 2021, and on November 24, 2021, Sonde issued unsecured convertible promissory notes to its existing shareholders for a combined total of $4.3 million, of which $2.2 million were issued to third party shareholders (and $2.1 million were issued to the Company and eliminated in consolidation). The notes bear interest at an annual rate of 6.0 percent and mature on the second anniversary of the issuance. The notes mandatorily convert in a Qualified Financing, as defined in the note purchase agreement, at a discount of 20.0 percent from the price per share in the Qualified Financing. In addition, the notes allow for optional conversion concurrently with the closing of a Non-Qualified Equity Financing to the Non-Qualified Equity Securities then issued and sold at a discount of 20.0 percent from the price per share in the Non Qualified Equity Financing. In the event of no conversion or repayment of the notes prior to a Change in Control, the notes shall become immediately due and payable prior to the closing of such Change in Control at three times the outstanding principal plus accrued interest.

For the Vedanta and Sonde convertible notes, since these Notes contain embedded derivatives, the Notes were assessed under IFRS 9 and the entire financial instruments were elected to be accounted for as FVTPL. The Vedanta convertible note was settled through its conversion in July 2021. See above. See Note 16 for further details on the fair value of the Sonde notes.

18. Non-Controlling Interest

During the year ended December 31, 2021, the Company acquired the non-controlling interest in Alivio which resulted in Alivio being transferred to the Internal segment. The Company has revised in the 2021 financial statements the prior period financial information related to the segmentation of NCI, to conform to the presentation as of and for the year ending December 31, 2021. Please refer to Note 4 "Segment Information" for further details regarding reportable segments.

The following table summarizes the changes in the equity classified non-controlling ownership interest in subsidiaries by reportable segment:

	Internal $000s	Controlled Founded Entities $000s	Non-Controlled Founded Entities $000s	Parent Company & Other $000s	Total $000s
Balance at January 1, 2019 *	(15,102)	(20,800)	(73,225)	592	(108,535)
Share of comprehensive loss	(17,643)	(13,483)	(23,953)	—	(55,079)
Deconsolidation of subsidiary	—	—	97,178	—	97,178
Subsidiary note conversion and changes in NCI ownership interest	—	23,049	—	—	23,049
Equity settled share-based payments	—	1,683	—	—	1,683
Acquisition of a subsidiary non controlling interest	24,039	—	—	—	24,039
Other	24	—	—	1	25
Balance at December 31, 2019 and January 1, 2020	(8,682)	(9,551)	—	593	(17,639)
Share of comprehensive loss	(191)	(1,211)	—	(15)	(1,417)
Equity settled share-based payments	305	2,517	—	—	2,822
Other	—	30	—	(6)	24
Balance at December 31, 2020 and January 1, 2021	(8,567)	(8,215)	—	574	(16,209)
Share of comprehensive income (loss)	(96)	(2,069)	—	15	(2,151)
NCI exercise of share-based awards in subsidiaries – change in NCI interest	—	(5,922)	—	—	(5,922)
Equity settled share-based payments	(4)	6,256	—	—	6,252
Acquisition of a subsidiary non controlling interest	8,668	—	—	—	8,668
Other	—	—	—	(6)	(6)
Balance as of December 31, 2021	**—**	**(9,950)**	**—**	**583**	**(9,368)**

(*) Revised to reclassify Alivio into the Internal segment to comply with current period classification. See Note 4.

The following tables summarize the financial information related to the Group's subsidiaries with material non-controlling interests, aggregated for interests in similar entities, and before and after intra group eliminations.

	2021				
For the year ended December 31	**Internal $000s**	**Controlled Founded Entities $000s**	**Non-Controlled Founded Entities $000s**	**Intra-group eliminations $000s**	**Total $000s**
Statement of Comprehensive Loss					
Total revenue	**—**	**7,771**	**—**	**—**	**7,771**
Income/(loss) for the year	**—**	**(50,436)**	**—**	**792**	**(49,644)**
Other comprehensive income/(loss)	**—**	**—**	**—**	**—**	**—**
Total comprehensive income/(loss) for the year	**—**	**(50,436)**	**—**	**792**	**(49,644)**
Statement of Financial Position					
Total assets	**—**	**66,279**	**—**	**(161)**	**66,118**
Total liabilities	**—**	**228,856**	**—**	**(10,755)**	**218,101**
Net assets/(liabilities)	**—**	**(162,576)**	**—**	**10,594**	**(151,982)**

As of December 31, 2021, Controlled Founded Entities with non-controlling interests primarily include Follica Incorporated, Sonde Health Inc., Entrega Inc. and Vedanta Biosciences, Inc. Ownership interests of the non-controlling interests in Follica Incorporated, Entrega Inc., Sonde Health Inc., and Vedanta Biosciences, Inc are 19.9 percent, 11.7 percent, 6.2 percent and 3.7 percent, respectively. In addition, Non-controlling interests include the amounts recorded for subsidiary stock options, with the vast majority comprising of Vedanta stock options.

18. Non-Controlling Interest — continued

For the year ended December 31	Internal $000s	Controlled Founded Entities $000s	Non-Controlled Founded Entities $000s	Intra-group eliminations $000s	Total $000s
			2020		
Statement of Comprehensive Loss					
Total revenue	3,267	1,957	—	—	5,224
Income/(loss) for the year	(2,407)	(53,535)	—	1,073	(54,869)
Total comprehensive income/(loss) for the year	(2,407)	(53,535)	—	1,073	(54,869)
Statement of Financial Position					
Total assets	1,297	67,048	—	(7)	68,339
Total liabilities	12,086	188,345	—	(14,621)	185,809
Net assets/(liabilities)	(10,788)	(121,296)	—	14,615	(117,470)

As of December 31, 2020, Internal segment with non-controlling interests include Alivio, Controlled Founded Entities with non-controlling interests primarily include, Follica Incorporated, Sonde Health Inc., and Vedanta Biosciences, Inc. Ownership interests of the non-controlling interests in Alivio Therapeutics, Inc., Follica Incorporated, Sonde Health Inc., and Vedanta Biosciences, Inc are 8.1 percent, 19.9 percent, 4.5 percent and 0.4 percent, respectively. In addition, Non-controlling interests include the amounts recorded for subsidiary stock options, with the vast majority comprising of Vedanta stock options.

For the year ended December 31	Internal $000s	Controlled Founded Entities $000s	Non-Controlled Founded Entities $000s
		2019	
Statement of Comprehensive Loss			
Total revenue	8,006	41	—
Income/(loss) for the year	(26,668)	(23,871)	(47,905)
Other comprehensive income/(loss)	—	—	(10)
Total comprehensive income/(loss) for the year	(26,668)	(23,871)	(47,915)

On July 19, 2019 PureTech and a third party investor converted their convertible debt in Follica to Follica Preferred shares (presented as liabilities) and Follica common shares. The amount of convertible debt converted by the third party investor into Follica common shares amounted to $2.4 million (see also Note 16). As a result of the conversion Follica NCI share (in Follica common stock) was reduced from 68 percent to 19.9 percent, which resulted in a reduction in the NCI share in Follica's shareholders' deficit of $19.9 million. The excess of the change in the book value of NCI ($19.9 million noted above) over the contribution made by NCI ($2.4 million) amounted to $17.5 million and was recorded as a loss directly in shareholders' equity.

During 2019 a subsidiary of the Company fully funded by the Company ceased its operations and became inactive. This resulted in a change in the NCI share in the subsidiary deficit. As a result the Company recorded a loss directly in equity of $3.1 million.

On October 1, 2019, PureTech acquired the remaining 10.0 percent of minority non-controlling interests of PureTech LYT, Inc. (previously named Ariya Therapeutics, Inc.), increasing its ownership from 90.0 percent to 100.0 percent. In consideration for the acquisition of minority interests, PureTech issued 2,126,338 shares of common shares. The fair value of the shares issued in consideration for the minority non-controlling interest amounted to $9.1 million. The carrying amount of the non-controlling interest at the acquisition was a $24.0 million deficit and the excess of the consideration paid over the book value of the non-controlling interest of approximately $33.1 million was recorded directly in shareholders' equity.

On June 11, 2021, PureTech acquired the remaining 17.1 percent of the minority non-controlling interests of Alivio (after exercise of all in the money stock options) increasing its ownership to 100.0 percent of Alivio. The consideration for such non controlling interests amounted to $1.2 million, to be paid in three equal installments, with the first installment of $0.4 million paid at the effective date of the transaction and two additional installment to be paid upon the occurrence of certain contingent events. The Group recorded a contingent consideration liability of $0.6 million at fair value for the two additional installments, resulting in a total acquisition cost of $1.0 million. The excess of the consideration paid over the book value of the non-controlling interest of approximately $9.6 million was recorded directly as a charge to shareholders' equity. The second installment of $0.4 million was paid in July 2021, upon the occurrence of the contingent event specified in the agreement. The contingent consideration liability is adjusted to fair value at the end of each reporting period with changes in fair value recorded in earnings. Changes in fair value of the aforementioned contingent consideration liability were not material.

On December 1, 2021, options holders in Entrega exercised options into shares of common stock, increasing the NCI interest held from 0.2 percent to 11.7 percent. During 2021 option holders in Vedanta exercised options and increased the NCI interest to 3.7 percent. The exercise of the options resulted in an increase in the NCI share in Entrega's and Vedanta's shareholder's deficit of $5.9 million. The consideration paid by NCI ($0.1 million) together with the increase in NCI share in Entrega's and Vedanta's shareholder deficit ($5.9 million) amounted to $6.0 million and was recorded as a gain directly in shareholders' equity.

19. Trade and Other Payables

Information regarding Trade and other payables was as follows:

As of December 31,	**2021 $000s**	2020 $000s
Trade payables	**11,346**	8,871
Accrued expenses	**17,309**	9,090
Income tax payable	**57**	1,260
Liability settled share based awards	**4,703**	—
Other	**2,403**	2,606
Total trade and other payables	**35,817**	21,826

20. Long-term loan

In September 2020, Vedanta entered into a $15.0 million loan and security agreement with Oxford Finance LLC. The loan is secured by Vedanta's assets, including equipment, inventory and intellectual property. The loan bears a floating interest rate of 7.7 percent plus the greater of (i) 30 day U.S. Dollar LIBOR reported in the Wall Street Journal or (ii) 0.17 percent. The loan matures September 2025 and requires interest only payments for the initial 24 months. The loan also carries a final fee upon full repayment of 7.0 percent of the original principal, or $1.1 million. For loan consideration, Vedanta also issued Oxford Finance LLC 12,886 Series C-2 preferred share warrants with an exercise price of $23.28 per share, expiring September 2030. The outstanding loan balance totaled approximately $15.1 million as of December 31, 2021.

The following table summarizes long-term loan activity for the years ended December 31, 2021 and 2020:

	Long-term loan	
	2021 $000s	2020 $000s
Balance at January 1,	**14,818**	—
Net loan proceeds	**—**	14,720
Accrued interest	**1,502**	496
Interest paid	**(1,201)**	(296)
Other	**—**	(102)
Balance at December 31,	**15,118**	14,818

The following table summarizes Vedanta's future principal payments for the long-term loan as of December 31, 2021:

Balance Type	2022	2023	2024	2025	Total
Principal	857	5,143	5,143	3,857	15,000
Balance of accreted premium net of unamortized issuance costs					118
Total					**15,118**

The long-term loan is presented as follows in the Statement of Financial Position as of December 31, 2021 and 2020:

	Long-term loan	
	2021 $000s	2020 $000s
Current portion of Long-term loan	**857**	—
Long-term loan	**14,261**	14,818
Total Long-term loan	**15,118**	14,818

21. Leases

The activity related to the Group's right of use asset and lease liability for the years ended December 31, 2021 and 2020 is as follows:

	Right of use asset, net	
	2021 $000s	2020 $000s
Balance at January 1,	**20,098**	22,383
Additions	**739**	—
Tenant improvement - lease incentive	**(733)**	—
Depreciation	**(2,938)**	(2,699)
Adjustments	**—**	414
Balance at December 31,	**17,166**	20,098

	Total lease liability	
	2021 $000s	2020 $000s
Balance at January 1,	**35,348**	37,843
Additions	**1,016**	—
Cash paid for rent - principal - financing cash flow	**(3,375)**	(2,908)
Cash paid for rent - interest	**(2,181)**	(2,354)
Interest expense	**2,181**	2,354
Adjustments	**—**	414
Balance at December 31,	**32,990**	35,348

Depreciation of the right-of-use assets, which virtually all consist of leased real estate, is included in the General and administrative expenses and Research and development expenses line items in the Consolidated Statements of Comprehensive Income/(Loss). The Company recorded depreciation expense of $2.9 million, $2.7 million and $3.2 million for the years ended December 31, 2021, 2020 and 2019, respectively.

The following details the short-term and long-term portion of the lease liability as at December 31, 2021 and 2020:

	Total lease liability	
	2021 $000s	2020 $000s
Short-term Portion of Lease Liability	**3,950**	3,261
Long-term Portion of Lease Liability	**29,040**	32,088
Total Lease Liability	**32,990**	35,348

The following table details the future maturities of the lease liability, showing the undiscounted lease payments to be paid after the reporting date:

	2021 $000s
Less than one year	**5,927**
One to two years	**6,591**
Two to three years	**6,754**
Three to four years	**5,168**
Four to five years	**4,419**
More than five years	**12,033**
Total undiscounted lease maturities	**40,893**
Interest	**7,903**
Total lease liability	**32,990**

During the year ended December 31, 2019, PureTech entered into a lease agreement for certain premises consisting of approximately 50,858 rentable square feet of space located at 6 Tide Street. The lease commenced on April 26, 2019 ("Commencement Date") for an initial term consisting of ten years and three months and there is an option to extend for two consecutive periods of five years each. The Company assessed at lease commencement date whether it is reasonably certain to exercise the extension options and deemed such options not reasonably certain to be exercised. The Company will reassess whether it is reasonably certain to exercise the options only if there is a significant event or significant changes in circumstances within its control.

21. Leases — continued

On June 26, 2019, PureTech executed a sublease agreement with Gelesis. The lease is for the approximately 9,446 rentable square feet located on the sixth floor of the Company's former offices at the 501 Boylston Street building. The sublessee obtained possession of the premises on June 1, 2019 and the rent period term began on June 1, 2019 and expires on August 31, 2025. The sublease was determined to be a finance lease. As of December 31, 2021, the balances related to the sublease were as follows:

	Total lease receivable $000s
Short-term Portion of Lease Receivable	415
Long-term Portion of Lease Receivable	1,285
Total Lease Receivable	**1,700**

The following table details the future maturities of the lease receivable, showing the undiscounted lease payments to be received after the reporting date:

	2021 $000s
Less than one year	**504**
One to two years	**513**
Two to three years	**523**
Three to four years	**353**
Total undiscounted lease receivable	**1,892**
Unearned Finance income	**192**
Net investment in the lease	**1,700**

On August 6, 2019, PureTech executed a sublease agreement with Dewpoint Therapeutics, Inc. ("Dewpoint"). The sublease was for approximately 11,852 rentable square feet located on the third floor of the 6 Tide Street building, where the Company's offices are currently located. Dewpoint obtained possession of the premises on September 1, 2019 with a rent period term that began on September 1, 2019, and expired on August 31, 2021. The sublease was determined to be an operating lease.

Rental income recognized by the Company during the years ended December 31, 2021, 2020 and 2019, was $0.65 million, $1.08 million and $0.4 million, respectively and is included in the Other income/(expense) line item in the Consolidated Statements of Comprehensive Income/(Loss).

22. Capital and Financial Risk Management

Capital Risk Management

The Group's capital and financial risk management policy is to maintain a strong capital base so as to support its strategic priorities, maintain investor, creditor and market confidence as well as sustain the future development of the business. The Group's objectives when managing capital are to safeguard its ability to continue as a going concern in order to provide returns for shareholders and benefits for other stakeholders and to maintain an optimal capital structure to reduce the cost of capital. To maintain or adjust the capital structure, the Group may issue new shares or incur new debt. The Group has some external debt and no material externally imposed capital requirements. The Group's share capital is clearly set out in Note 14.

Management continuously monitors the level of capital deployed and available for deployment in the Internal and Parent segments as well as at Controlled Founded Entities. The Directors seek to maintain a balance between the higher returns that might be possible with higher levels of deployed capital and the advantages and security afforded by a sound capital position.

The Group's Directors have overall responsibility for establishment and oversight of the Group's capital and risk management framework. The Group is exposed to certain risks through its normal course of operations. The Group's main objective in using financial instruments is to promote the development and commercialization of intellectual property through the raising and investing of funds for this purpose. The Group's policies in calculating the nature, amount and timing of investments are determined by planned future investment activity. Due to the nature of activities and with the aim to maintain the investors' funds as secure and protected, the Group's policy is to hold any excess funds in highly liquid and readily available financial instruments and maintain insignificant exposure to other financial risks.

COVID-19

In March 2020, the World Health Organization declared the COVID-19 outbreak a pandemic. The pandemic has since caused widespread and significant disruption to daily life and the global economy as governments have taken actions, including the issuance of stay-at-home orders and social distancing guidelines, and businesses have adjusted their activities. While our business, operations and financial condition and results have not been significantly impacted in 2020 or 2021, as a result of the COVID-19 pandemic, we have taken swift action to ensure the safety of our employees and other stakeholders. The Group continues to monitor the latest developments regarding the COVID-19 pandemic on business, operations, and financial condition and results, and has made certain assumptions regarding the pandemic for purposes of the Group's operational planning and financial projections, including assumptions regarding the duration and severity of the pandemic and the global macroeconomic impact of the pandemic. Despite careful tracking and planning, however, the Group is unable to accurately predict the extent of the impact of the pandemic on the business, operations, and financial condition and results in future periods due to the uncertainty of future developments. The Group is focused on all aspects of the business and is implementing measures aimed at mitigating issues where possible.

22. Capital and Financial Risk Management — continued

Credit Risk

The Group has exposure to the following risks arising from financial instruments:

Credit risk is the risk of financial loss to the Group if a customer or counterparty to a financial instrument fails to meet its contractual obligations. Financial instruments that potentially subject the Group to concentrations of credit risk consist principally of cash and cash equivalents and trade and other receivables. The Group held the following balances (not including the income tax receivable resulting from overpayment of income taxes, see Note 25):

As of December 31	**2021 $000s**	2020 $000s
Cash and cash equivalents	**465,708**	403,881
Trade and other receivables	**3,174**	2,558
Total	**468,882**	406,438

The Group invests its excess cash in U.S. Treasury Bills, U.S. debt obligations and money market accounts, which the Group believes are of high credit quality. Further the Group's cash and cash equivalents and short-term investment are held at diverse, investment-grade financial institutions.

The Group assesses the credit quality of customers on an ongoing basis. The credit quality of financial assets is assessed by historical and recent payment history, counterparty financial position, reference to credit ratings (if available) or to historical information about counterparty default rates. The Group does not have expected credit losses owing largely to a small number of counterparties and the high credit quality of such counterparties (primarily the US government and large funds in respect of grant income).

The aging of trade and other receivables that were not impaired at December 31 is as follows:

As of December 31	**2021 $000s**	2020 $000s
Not impaired	**3,174**	2,558
Total	**3,174**	2,558

Liquidity Risk

Liquidity risk is the risk that the Group will encounter difficulty in meeting the obligations associated with its financial liabilities that are settled by delivering cash or another financial asset. The Group actively manages its risk of a funds shortage by closely monitoring the maturity of its financial assets and liabilities and projected cash flows from operations, under both normal and stressed conditions, without incurring unacceptable losses or risking damage to the Group's reputation. Due to the nature of these financial liabilities, the funds are available on demand to provide optimal financial flexibility.

The table below summarizes the maturity profile of the Group's financial liabilities, including subsidiary preferred shares that have customary liquidation preferences, as of December 31, 2021 and 2020, based on contractual undiscounted payments:

	2021				
As of December 31	**Carrying Amount $000s**	**Within Three Months $000s**	**Three to Twelve Months $000s**	**One to Five Years $000s**	**Total $000s (*)**
Long-term loan (non-current + current)	**15,118**	**296**	**2,182**	**16,274**	**18,752**
Subsidiary notes payable	**3,916**	**3,916**	**—**	**—**	**3,916**
Trade and other payables	**35,817**	**35,817**	**—**	**—**	**35,817**
Warrants[2]	**6,787**	**6,787**	**—**	**—**	**6,787**
Subsidiary preferred shares (Note 15)[1]	**174,017**	**174,017**	**—**	**—**	**174,017**
Total	**235,656**	**220,833**	**2,182**	**16,274**	**239,290**

	2020				
As of December 31	Carrying Amount $000s	Within Three Months $000s	Three to Twelve Months $000s	One to Five Years $000s	Total $000s (*)
Long-term loan	14,818	296	905	18,780	19,981
Subsidiary notes payable	26,455	1,455	25,000	—	26,455
Trade and other payables	21,826	21,826	—	—	21,826
Warrants[2]	8,206	8,206	—	—	8,206
Subsidiary preferred shares (Note 15)[1]	118,972	118,972	—	—	118,972
Total	190,278	150,756	25,905	18,780	195,441

1 Redeemable only upon a liquidation or Deemed liquidation event, as defined in the applicable shareholder documents.

2 Warrants issued by subsidiaries to third parties to purchase preferred shares.

(*) Does not include payments in respect of lease obligations. For the contractual future payments related to lease obligations, see Note 21.

22. Capital and Financial Risk Management — continued

Interest Rate Sensitivity

As of December 31, 2021, the Group had cash and cash equivalents of $465.7 million. The Group's exposure to interest rate sensitivity is impacted by changes in the underlying U.K. and U.S. bank interest rates. The Group has not entered into investments for trading or speculative purposes. Due to the conservative nature of the Group's investment portfolio, which is predicated on capital preservation and investments in short duration, high-quality U.S. Treasury Bills and U.S. debt obligations and related money market accounts, a change in interest rates would not have a material effect on the fair market value of the Group's portfolio, and therefore the Group does not expect operating results or cash flows to be significantly affected by changes in market interest rates.

Controlled Founded Entity Investments

The Group maintains investments in certain Controlled Founded Entities. The Group's investments in Controlled Founded Entities are eliminated as intercompany transactions upon financial consolidation. The Group is however exposed to a preferred share liability owing to the terms of existing preferred shares and the ownership of Controlled Founded Entities preferred shares by third parties. As discussed in Note 15, certain of the Group's subsidiaries have issued preferred shares that include the right to receive a payment in the event of any voluntary or involuntary liquidation, dissolution or winding up of a subsidiary, including in the event of "deemed liquidation" as defined in the incorporation documents of the entities, which shall be paid out of the assets of the subsidiary available for distribution to shareholders and before any payment shall be made to holders of ordinary shares. The liability of preferred shares is maintained at fair value through the profit and loss. The Group's strong cash position, budgeting and forecasting processes, as well as decision making and risk mitigation framework enable the Group to robustly monitor and support the business activities of the Controlled Founded Entities to ensure no exposure to dissolution or liquidation. Accordingly, the Group views exposure to 3rd party preferred share liability as low.

Non-Controlled Founded Entity Investments

The Group maintains certain investments in Non-Controlled Founded Entities which are deemed either as investments and accounted for as investments held at fair value or associates and accounted for under the equity method (please refer to Note 1). The Group's exposure to investments held at fair value is $397.2 million as of December 31, 2021, and the Group may or may not be able to realize the value in the future. Accordingly, the Group views the risk as high. The Group's exposure to investments in associates is limited to the carrying amount of the investment in an Associate. The Group is not exposed to further contractual obligations or contingent liabilities beyond the value of initial investment. As of December 31, 2021, Gelesis was the only associate. The carrying amount of the investment in Gelesis as an associate was zero. Accordingly, the Group does not view this as a risk. Please refer to Notes 5,6 and 16 for further information regarding the Group's exposure to Non-Controlled Founded Entity Investments.

Equity Price Risk

As of December 31, 2021, the Group held 1,656,564 common shares of Karuna and 3,207,200 common shares of Vor. The fair value of the Group's investment in the common stock of Karuna and Vor was $217.0 million and $37.3 million respectively.

The investments in Karuna and Vor are exposed to fluctuations in the market price of these common shares. The effect of a 10.0 percent adverse change in the market price of Karuna and Vor common shares as of December 31, 2021, would have been a loss of approximately $21.7 million and $3.7 million respectively, recognized as a component of Other income (expense) in the Consolidated Statements of Comprehensive Income/(Loss).

Foreign Exchange Risk

The Group maintains consolidated financial statements in the Group's functional currency, which is the U.S. dollar. Monetary assets and liabilities denominated in currencies other than the functional currency are translated into the functional currency at rates of exchange prevailing at the balance sheet dates. Non-monetary assets and liabilities denominated in foreign currencies are translated into the functional currency at the exchange rates prevailing at the date of the transaction. Exchange gains or losses arising from foreign currency transactions are included in the determination of net income (loss) for the respective periods. Such foreign currency gains or losses were not material for all reported periods. See Note 9.

The Group does not currently engage in currency hedging activities since its foreign currency risk is limited, but the Group may begin to do so in the future if and when its foreign currency risk exposure changes. Instruments that may be used to hedge future risks include foreign currency forward and swap contracts. These instruments may be used to selectively manage risks, but there can be no assurance that the Group will be fully protected against material foreign currency fluctuations.

23. Commitments and Contingencies

The Group is party to certain licensing agreements where the Group is licensing IP from third parties. In consideration for such licenses the Group has made upfront payments and may be required to make additional contingent payments based on developmental and sales milestones and/or royalty on future sales. As of December 31, 2021, these milestone events have not yet occurred and therefore the Group does not have a present obligation to make the related payments in respect of the licenses. Such milestones are dependent on events that are outside of the control of the Group and many of these milestone events are remote of occurring. As of December 31, 2021, payments in respect of developmental milestones that are dependent on events that are outside the control of the Group but are reasonably possible to occur amounted to approximately $10.3 million. These milestone amounts represent an aggregate of multiple milestone payments depending on different milestone events in multiple agreements. The probability that all such milestone events will occur in the aggregate is remote. Payments made to license IP represent the acquisition cost of intangible assets. See Note 12.

The Group is party to certain sponsored research arrangements as well as arrangements with contract manufacturing and contract research organizations, whereby the counterparty provides the Company with research and/or manufacturing services. As of December 31, 2021, the noncancellable commitments in respect of such contracts amounted to approximately $6.7 million.

24. Related Parties Transactions

Related Party Subleases and royalties

During 2019, PureTech executed sublease agreements with a related party, Gelesis. Please refer to Note 21 for further details regarding the sublease.

The Group receives royalties from Gelesis on its product sales. Such royalties amounted to $231 thousand and $54 thousand for the years ended December 31, 2021 and 2020, respectively and are presented in Contract revenue in the Consolidated Statements of Comprehensive Income/(Loss).

Key Management Personnel Compensation

Key management includes executive directors and members of the executive management team of the Group (not including compensation provided to independent directors). Full details for Directors' remuneration can be found in the Directors' Remuneration Report. The key management personnel compensation of the Group was as follows for the years ended December 31:

As of December 31	**2021 $000s**	2020 $000s	2019 $000s
Short-term employee benefits	**4,666**	4,833	5,543
Share-based payments	**4,045**	5,822	2,774
Total	**8,711**	10,656	8,317

Short-term employee benefits include salaries, health care and other non-cash benefits. Share-based payments are generally subject to vesting terms over future periods.

For cash settlements of share based awards – see Note 8.

During the year ended December 31, 2021, the company incurred $782 thousand of general administrative expenses that was paid to a related party.

Convertible Notes Issued to Directors

Certain members of the Group have invested in convertible notes issued by the Group's subsidiaries. As of December 31, 2021, 2020 and 2019, the outstanding related party notes payable totaled $94 thousand, $89 thousand and $84 thousand respectively, including principal and interest.

The notes issued to related parties bear interest rates, maturity dates, discounts and other contractual terms that are the same as those issued to outside investors during the same issuances, as described in Note 17.

24. Related Parties Transactions — continued

Directors' and Senior Managers' Shareholdings and Share Incentive Awards

The Directors and senior managers hold beneficial interests in shares in the following businesses and sourcing companies as at December 31, 2021:

	Business Name (Share Class)	Number of shares held as of December 31, 2021	Number of options held as of December 31, 2021	Ownership Interest[1]
Directors:				
Ms. Daphne Zohar[2]	Gelesis (Common)	**179,443**	**1,207,006**	**5.03%**
Dr. Robert Langer	Entrega (Common)	**250,000**	**82,500**	**4.09%**
Dr. Raju Kucherlapati	Enlight (Class B Common)	**—**	**30,000**	**3.00%**
Dr. John LaMattina[3]	Akili (Series A-2 Preferred)	**37,372**	**—**	**0.80%**
	Akili (Series C Preferred)	**11,755**	**—**	**0.20%**
	Gelesis (Common)[3]	**50,540**	**—**	**0.18%**
	Gelesis (Common)[4]	**33,051**	**33,578**	**0.24%**
	Gelesis (Series A-1 Preferred)[3]	**49,523**	**—**	**0.18%**
	Vedanta Biosciences (Common)	**25,000**	**—**	**0.17%**
Senior Managers:				
Dr. Bharatt Chowrira	Karuna (Common)[4]	**5,000**	**—**	**0.02%**
Dr. Joseph Bolen	Vor (Common)	**—**	**9,191**	**0.02%**

1 Ownership interests as of December 31, 2021 are calculated on a diluted basis, including issued and outstanding shares, warrants and options (and written commitments to issue options) but excluding unallocated shares authorized to be issued pursuant to equity incentive plans and any shares issuable upon conversion of outstanding convertible promissory notes.

2 Common shares and options held by Yishai Zohar, who is the husband of Ms. Zohar. Ms. Zohar does not have any direct interest in the share capital of Gelesis. Ms. Zohar recuses herself from any and all material decisions with regard to Gelesis.

3 Dr. John and Ms. Mary LaMattina hold 50,540 shares of common shares and 49,523 shares of Series A-1 preferred shares in Gelesis. Individually, Dr. LaMattina holds 33,051 shares of Gelesis and convertible notes issued by Appeering in the aggregate principal amount of $50,000.

4 Options to purchase the listed shares were granted in connection with the service on such founded entity's Board of Directors and any value realized therefrom shall be assigned to PureTech Health, LLC.

Directors and senior managers hold 24,676,165 ordinary shares and 8.6 percent voting rights of the Company as of December 31, 2021. This amount excludes options to purchase 4,750,000 ordinary shares. This amount also excludes 4,666,514 shares, which are issuable based on the terms of performance based RSU awards granted to certain senior managers covering the financial years 2021, 2020 and 2019, and 67,140 shares, which are issuable to directors immediately prior to the Company's 2022 Annual General Meeting of Stockholders based on the terms of the RSU awards granted to non-executive directors in 2021. Such shares will be issued to such senior managers and non executive directors in future periods provided that performance and/or service conditions are met and certain of the shares will be withheld for payment of customary withholding taxes.

Short term Note from Associate

See Note 16 for details on the $15.0 million note issued by Gelesis to the Company. The Company recognized income of $0.1 million with respect to interest and changes in fair value related to the short term note.

25. Taxation

Tax on the profit or loss for the year comprises current and deferred income tax. Tax is recognized in the Consolidated Statements of Comprehensive Income/(Loss) except to the extent that it relates to items recognized directly in equity.

For the years ended December 31, 2021, 2020 and 2019, the Group filed a consolidated U.S. federal income tax return which included all subsidiaries in which the Company owned greater than 80 percent of the vote and value. For the years ended December 31, 2021, 2020 and 2019, the Group filed certain consolidated state income tax returns which included all subsidiaries in which the Company owned greater than 50 percent of the vote and value. The remaining subsidiaries file separate U.S. tax returns.

Amounts recognized in Consolidated Statements of Comprehensive Income/(Loss):

As of December 31	**2021 $000s**	2020 $000s	2019 $000s
Income/(loss) for the year	**(62,709)**	4,568	366,065
Income tax expense/(benefit)	**3,756**	14,401	112,409
Income/(loss) before taxes	**(58,953)**	18,969	478,474

Recognized income tax expense/(benefit):

As of December 31	**2021 $000s**	2020 $000s	2019 $000s
Federal	**22,138**	21,796	—
Foreign	**—**	—	—
State	**109**	—	—
Total current income tax expense/(benefit)	**22,247**	21,796	—
Federal	**(15,416)**	(7,349)	83,776
Foreign	**—**	—	—
State	**(3,075)**	(46)	28,633
Total deferred income tax expense/(benefit)	**(18,491)**	(7,395)	112,409
Total income tax expense/(benefit), recognized	**3,756**	14,401	112,409

The tax expense was $3.8 million, $14.4 million and $112.4 million in 2021, 2020 and 2019 respectively. The decrease in tax expense is primarily the result of the decrease in profit before tax in entities in the U.S. Federal and Massachusetts consolidated return groups of the Company.

Reconciliation of Effective Tax Rate

The Group is primarily subject to taxation in the U.S. A reconciliation of the U.S. federal statutory tax rate to the effective tax rate is as follows:

	2021		2020		2019	
As of December 31	**$000s**	**%**	$000s	%	$000s	%
US federal statutory rate	**(12,380)**	**21.00**	3,984	21.00	97,183	21.00
Effects of state tax rate in U.S.	**(4,484)**	**7.61**	1,844	9.72	22,111	4.78
R&D and orphan drug tax credits	**(5,056)**	**8.58**	(5,642)	(29.74)	(6,321)	(1.37)
Non deductible share based payment expenses	**555**	**(0.94)**	327	1.73	433	0.09
Finance income/(costs) – fair value accounting	**(2,017)**	**3.42**	919	4.84	3,725	0.80
Loss with respect to associate for which no deferred tax asset is recognized	**11,542**	**(19.58)**	—	—	—	—
Transaction Costs	**309**	**(0.52)**	361	1.91	—	—
Interest Expense	**217**	**(0.37)**	(2,258)	(11.91)	1,030	0.22
Executive Compensation	**746**	**(1.27)**	827	4.36	—	—
Deconsolidation adjustments	**—**	**0.00**	—	—	(13,658)	(2.95)
Recognition of deferred tax assets and tax benefits not previously recognized	**(414)**	**0.70**	—	—	(6,251)	(1.35)
Current year losses for which no deferred tax asset is recognized	**14,375**	**(24.38)**	13,948	73.53	14,514	3.14
Other	**363**	**(0.62)**	91	0.48	(356)	(0.06)
	3,756	**(6.37)**	14,401	75.92	112,409	24.29

The Company is also subject to taxation in the UK but to date no taxable income has been generated in the UK. Changes in corporate tax rates can change both the current tax expense (benefit) as well as the deferred tax expense (benefit).

25. Taxation — continued

Deferred Tax Assets and Liabilities

Deferred tax assets have been recognized in the U.S. jurisdiction in respect of the following items:

As of December 31	**2021 $000s**	2020 $000s
Operating tax losses	**46,982**	39,901
Tax credits	**10,673**	10,805
Share-based payments	**7,265**	5,429
Deferred revenue	**—**	358
Investment in Associates	**11,542**	—
Lease Liability	**8,969**	9,657
Other temporary differences	**2,665**	2,078
Deferred tax assets	**88,096**	68,228
Investments held at fair value	**(96,804)**	(120,676)
ROU asset	**(4,667)**	(5,491)
Fixed assets	**(3,547)**	(3,588)
Other temporary differences	**—**	(27)
Deferred tax liabilities	**(105,018)**	(129,782)
Deferred tax assets (liabilities), net	**(16,922)**	(61,554)
Deferred tax liabilities, net, recognized	**(89,765)**	(108,626)
Deferred tax assets, net, recognized	**—**	—
Deferred tax assets (liabilities), net, not recognized	**72,843**	47,072

We have recognized deferred tax assets related to entities in the U.S. Federal and Massachusetts consolidated return groups due to future reversals of existing taxable temporary differences that will be sufficient to recover the net deferred tax assets. Our unrecognized deferred tax assets of $72.8 million are primarily related to tax credit, loss carryforwards and deductible temporary differences in subsidiaries outside the U.S. Federal and Massachusetts consolidated return groups. Such deferred tax assets have not been recognized because it is not probable that future taxable profits will be available to support their realizability. The unrecognized deferred tax assets, to a lesser extent, also relate to unrecognized deferred tax assets with respect to an investment in an associate since the Group does not believe it is probable that such tax benefits will be realized in the foreseeable future.

There was movement in deferred tax recognized, which impacted income tax expense by approximately $18.5 million benefit, primarily related to changes in the value of investments. The Company sold a portion of its stock in Karuna during 2021 and was able to partially offset its gains by using various attributes (i.e. net operating losses, research and development credits, etc.) resulting in current tax expense of $22.2 million.

Unrecognized Deferred Tax Assets

Deferred tax assets have not been recognized in respect of the following carryforward losses, credits and temporary differences, because it is not probable that future taxable profit will be available against which the Group can use the benefits therefrom.

	2021 $000s		2020 $000s	
As of December 31	**Gross Amount**	**Tax Effected**	Gross Amount	Tax Effected
Deductible Temporary Difference	**59,925**	**16,224**	7,997	1,679
Tax Losses	**215,425**	**46,982**	169,731	36,273
Tax Credits	**9,636**	**9,636**	9,120	9,120
Total	**284,986**	**72,843**	186,848	47,072

Tax Losses and tax credits carryforwards

Tax losses and tax credits for which no deferred tax asset was recognized

	2021 $000s		2020 $000s	
As of December 31	**Gross Amount**	**Tax Effected**	Gross Amount	Tax Effected
Tax losses expiring:				
Within 10 years	**19,735**	**4,343**	12,530	2,760
More than 10 years	**47,937**	**11,611**	55,312	12,117
Available Indefinitely	**147,753**	**31,028**	101,889	21,397
Total	**215,425**	**46,982**	169,731	36,273
Tax credits expiring:				
Within 10 years	**4**	**4**	13	13
More than 10 years	**9,632**	**9,632**	9,107	9,107
Available indefinitely	**—**	**—**	—	—
Total	**9,636**	**9,636**	9,120	9,120

25. Taxation — continued

The Group had U.S. federal net operating losses carry forwards ("NOLs") of approximately $215.4 million, $169.7 million and $243.0 million as of December 31, 2021, 2020 and 2019, respectively, which are available to offset future taxable income. These NOLs expire through 2037 with the exception of $147.8 million which is not subject to expiration. The Group had U.S. Federal research and development tax credits of approximately $3.9 million, $3.9 million and $7.4 million as of December 31, 2021, 2020 and 2019, respectively, which are available to offset future taxes that expire at various dates through 2041. The Group also had Federal Orphan Drug credits of approximately $5.7 million and $5.2 million as of December 31, 2021, and 2020, which are available to offset future taxes that expire at various dates through 2041. A portion of these Federal NOLs and credits can only be used to offset the profits from the Company's subsidiaries who file separate Federal tax returns. These NOLs and credits are subject to review and possible adjustment by the Internal Revenue Service.

The Group had Massachusetts net operating losses carry forwards ("NOLs") of approximately $27.9 million, $67.4 million and $273.0 million for the years ended December 31, 2021, 2020 and 2019, respectively, which are available to offset future taxable income. These NOLs expire at various dates beginning in 2030. The Group had Massachusetts research and development tax credits of approximately $1.3 million, $2.1 million and $1.6 million for the years ended December 31, 2021, 2020 and 2019, respectively, which are available to offset future taxes and expire at various dates through 2036. These NOLs and credits are subject to review and possible adjustment by the Massachusetts Department of Revenue.

Utilization of the NOLs and research and development credit carryforwards may be subject to a substantial annual limitation under Section 382 of the Internal Revenue Code of 1986 due to ownership change limitations that have occurred previously or that could occur in the future. These ownership changes may limit the amount of NOL and research and development credit carryforwards that can be utilized annually to offset future taxable income and tax, respectively. The Company notes that a 382 analysis was performed through December 31, 2021. The results of this analysis concluded that certain net operating losses were subject to limitation under Section 382 of the Internal Revenue Code. None of the Company's tax attributes which are subject to a restrictive Section 382 limitation have been recognized in the financial statements.

Tax Balances

The current tax related balances are presented in the Statement of Financial Position as follows:

As of December 31	**2021 $000s**	2020 $000s
Income tax receivable - current	**4,514**	—
Trade and Other Payables	**(57)**	(1,260)

Uncertain Tax Positions

The Company has no uncertain tax positions as of December 31, 2021. U.S. corporations are routinely subject to audit by federal and state tax authorities in the normal course of business.

26. Subsequent Events

The Company has evaluated subsequent events after December 31, 2021, the date of issuance of the Consolidated Financial Statements, and has not identified any recordable or disclosable events not otherwise reported in these Consolidated Financial Statements or notes thereto, except for the following:

On January 13, 2022 Gelesis completed its business combination with Capstar Special Purpose Acquisition Corp ("Capstar"). As part of the business combination all shares held in Gelesis, common and preferred, were exchanged for common shares of the merged entity. In addition, the Group invested $15.0 million in the class A common shares of Capstar as part of the PIPE transaction that took place immediately prior to the closing of the business combination and an additional approximately $5.0 million, as part of the Backstop agreement signed with Capstar on December 30, 2021 (see Note 6). Pursuant to the business combination, Gelesis became a wholly-owned subsidiary of Capstar and Capstar changed its name to Gelesis Holdings, Inc., which began trading on the New York Stock exchange under the ticker symbol "GLS" on January 14, 2022. Following the closing of the business combination, the PIPE transaction and the settlement of the aforementioned Backstop agreement with Capstar, PureTech holds 16,727,582 common shares of Gelesis Holdings Inc., which is equal to approximately 23.2% of Gelesis Holdings Inc's outstanding common shares.

On January 26, 2022, Akili Interactive and Social Capital Suvretta Holdings Corp a special purpose acquisition company announced they had entered into a definitive business combination agreement. Upon completion of the transaction, the combined company's securities are expected to be traded on the Nasdaq Stock Market under the ticker symbol "AKLI". The transaction is expected to close in mid-2022. As part of this transaction the Akili Interactive shares held by the Company will be exchanged for the combined company's securities and the Company's interest in the combined public entity is expected to decrease from its current voting interest in Akili of 26.7%.

PureTech Health plc Statement of Financial Position

For the years ended December 31

	Note	2021 $000s	2020 $000s
Assets			
Non-current assets			
Investment in subsidiary	2	**148,086**	161,082
Intercompany long-term receivable	3	**297,909**	297,556
Total non-current assets		**445,995**	458,638
Total current assets		**—**	—
Total assets		**445,995**	458,638
Equity and liabilities			
Equity			
Share capital	4	**5,444**	5,417
Share premium	4	**289,304**	288,978
Merger reserve	4	**138,506**	138,506
Other reserve	4	**7,730**	20,725
Accumulated deficit (Income/(loss) for the year $(3,401))	4	**(14,022)**	(10,621)
Total equity		**426,961**	443,005
Current liabilities			
Trade and other payables		**1,856**	621
Intercompany payables	5	**17,179**	15,012
Total current liabilities		**19,034**	15,633
Total equity and liabilities		**445,995**	458,638

Please refer to the accompanying Notes to the PureTech Health plc financial information. Registered number: 09582467.

The PureTech Health plc financial statements were approved by the Board of Directors and authorized for issuance on April 25, 2022 and signed on its behalf by:

Daphne Zohar
Chief Executive Officer

April 25, 2022

The accompanying Notes are an integral part of these financial statements.

PureTech Health plc Statements of Cash Flows

For the years ended December 31

	2021 $000s	2020 $000s
Cash flows from operating activities		
Net loss	**(3,401)**	(2,739)
Adjustments to reconcile net operating loss to net cash used in operating activities:		
Non-cash items:		
Changes in operating assets and liabilities:		
Intercompany payable	**2,167**	3,354
Accounts payable and accrued expenses	**465**	(614)
Net cash (used in) operating activities	**(770)**	—
Cash flows from investing activities:		
Net cash provided by (used in) investing activities	**—**	—
Cash flows from financing activities:		
Net cash provided by (used in) financing activities	**—**	—
Net decrease in cash and cash equivalents	**(770)**	—
Cash and cash equivalents at beginning of year	**—**	—
Cash and cash equivalents at end of year	**(770)**	—
Supplemental disclosure of non-cash investment and financing activities:		
Increase (Decrease) in investment against share-based awards	**(12,995)**	19,734
Exercise of share-based awards against intercompany receivable	**352**	1,025

The accompanying Notes are an integral part of these financial statements.

PureTech Health plc Statements of Changes in Equity

For the years ended December 31

	Shares	Amount $000s	Share Premium $000s	Merger Reserve $000s	Other Reserve $000s	Accumulated deficit $000s	Total equity $000s
Balance January 1, 2020	**285,370,619**	**5,408**	**287,962**	**138,506**	**991**	**(7,881)**	**424,986**
Total comprehensive loss for the period							—
Exercise of share-based awards	514,406	9	1,016	—	—	—	1,025
Settlement of restricted stock units	—	—	—	—	(12,888)	—	(12,888)
Equity settled share-based payments	—	—	—	—	33,902	—	33,902
Vesting of restricted stock units	—	—	—	—	(1,280)	—	(1,280)
Net loss	—	—	—	—	—	(2,739)	(2,739)
Balance December 31, 2020	**285,885,025**	**5,417**	**288,978**	**138,506**	**20,725**	**(10,620)**	**443,005**
Total comprehensive loss for the period							
Exercise of share-based awards	1,911,560	27	326	—	—	—	352
Equity settled share-based awards	—	—	—	—	7,109	—	7,109
Settlement of restricted stock units	—	—	—	—	(10,749)	—	(10,749)
Vesting of share-based awards and net share exercise	—	—	—	—	(2,582)	—	(2,582)
Reclassification of equity settled awards to liability awards in subsidiary	—	—	—	—	(6,773)	—	(6,773)
Net loss	—	—	—	—	—	(3,401)	(3,401)
Balance December 31, 2021	**287,796,585**	**5,444**	**289,303**	**138,506**	**7,730**	**(14,022)**	**426,961**

The accompanying Notes are an integral part of these financial statements.

Notes to the Financial Statements

1. Accounting policies

Basis of Preparation and Measurement

The financial statements of PureTech Health plc (the "Parent") are presented as of December 31, 2021 and 2020, and for the years ended December 31, 2021 and 2020, and have been prepared under the historical cost convention in accordance with international accounting standards in conformity with the requirements of UK-adopted International Financial Reporting Standards (IFRSs). The financial statements of PureTech Health plc also comply fully with IFRSs as issued by the International Accounting Standards Board (IASB). A summary of the significant accounting policies that have been applied consistently throughout the year are set out below.

Functional and Presentation Currency

The functional currency of the Parent is United States ("U.S.") Dollars and the financial statements are presented in U.S. Dollars.

Investments

Investments are stated at historic cost less any provision for impairment in value and are held for long-term investment purposes. Provisions are based upon an assessment of events or changes in circumstances that indicate that an impairment has occurred such as the performance and/or prospects (including the financial prospects) of the investee company being significantly below the expectations on which the investment was based, a significant adverse change in the markets in which the investee company operates or a deterioration in general market conditions.

Impairment

If there is an indication that an asset might be impaired, the Parent would perform an impairment review. An asset is impaired if the recoverable amount, being the higher of net realizable value and value in use, is less than its carrying amount. Value in use is measured based on future discounted cash flows attributable to the asset. In such cases, the carrying value of the asset is reduced to recoverable amount with a corresponding charge recognized in the profit and loss account.

Financial Instruments

Currently the Parent does not enter into derivative financial instruments. Financial assets and financial liabilities are recognized and cease to be recognized on the basis of when the related titles pass to or from the Parent Company.

Equity Settled Share Based Payments

Share based payment awards granted in subsidiaries to employees and consultants to be settled in Parent's equity instruments are accounted for as equity-settled share-based payment transactions in accordance with IFRS 2. The grant date fair value of employee share-based payment awards granted in subsidiaries is recognized as an increase to the investment with a corresponding increase in equity over the requisite service period related to the awards. The fair value is measured using an option pricing model, which takes into account the terms and conditions of the options granted. When the subsidiary settles the equity awards other than by the Parent's equity the settlement is recorded as a decrease in equity against a corresponding decrease to the investment account.

2. Investment in subsidiary

	$000s
Balance at May 8, 2015	—
Investment in PureTech LLC as a result of the reverse acquisition	**141,348**
Increase due to equity settled share based payments granted to employees and service providers in subsidiaries	**19,734**
Balance at December 31, 2020	**161,082**
Decrease due to equity settled share based payments granted to employees and service providers in subsidiaries	**(12,996)**
Balance at December 31, 2021	**148,086**

PureTech consists of the Parent and its subsidiaries (together, the "Group"). Investment in subsidiary represents the Parent's investment in PureTech LLC as a result of the reverse acquisition of the Group's financial statements immediately prior to the Parent's initial public offering ("IPO") on the London Stock Exchange in June 2015. PureTech LLC operates in the U.S. as a US-focused scientifically driven research and development company that conceptualizes, sources, validates and commercializes unexpected and potentially disruptive approaches to advance the needs of human health. For a summary of the Parent's indirect subsidiaries please refer to Note 1 of the Consolidated Financial Statements of PureTech Health plc.

In 2020, the Parent recognized a $19.7 million increase in its investment in its operating subsidiary PureTech LLC due to equity settled share based payments granted to employees and service providers in subsidiaries. $24.8 million out of such amount related to amounts which should have been recognized at December 31, 2019. The prior year balance sheet has not been adjusted since the Directors do not believe this item is qualitatively material to users of the financial statements, it has no impact on distributable reserves of the Parent and no impact on the Group consolidated financial statements. The disclosure relating to such share based payment awards is detailed in Note 8 of the accompanying Consolidated Financial Statements. The decrease in 2021 due to such equity settled share based payments results from settlements and payments of these equity awards by the subsidiaries, net of the expense related to the grant of such equity settled share based awards.

3. Intercompany receivables

The Parent has an accounts receivable balance from its operating subsidiary PureTech LLC of $297.9 million as of December 31, 2021 due to cash received from the IPO and other share issuances.

As of December 31, 2021and 2020, the intercompany receivable balance was classified as a long-term receivable since the Parent does not expect to realize the receivable within the next 12 months.

4. Share capital and reserves

PureTech plc was incorporated with the Companies House under the Companies Act 2006 as a public company on May 8, 2015.

On March 12, 2018, the Company raised approximately $100.0 million, before issuance costs and other expenses, by way of a Placing of 45,000,000 placing shares.

On June 24, 2015, the Company authorized 227,248,008 of ordinary share capital at one pence apiece. These ordinary shares were admitted to the premium listing segment of the United Kingdom's Listing Authority and traded on the Main Market of the London Stock Exchange for listed securities. In conjunction with the authorization of the ordinary shares, the Parent completed an IPO on the London Stock Exchange, in which it issued 67,599,621 ordinary shares at a public offering price of 160 pence per ordinary share, in consideration for$159.3 million, net of issuance costs of $11.8 million.

Additionally, the IPO included an over-allotment option equivalent to 15 percent of the total number of new ordinary shares. The stabilization manager provided notice to exercise in full its over-allotment option on July 2, 2015. As a result, the Parent issued 10,139,943 ordinary shares at the offer price of 160 pence per ordinary share, which resulted in net proceeds of $24.2 million, net of issuance costs of $0.8 million.

During the years ended December 31, 2020 and 2021, Other reserves increased (decreased) by $19.7 million and $(13.0) million respectively due to equity settled share based payments granted to employees and service providers in subsidiaries. See Note 2 above.

5. Intercompany payables

The Parent has a balance due to its operating subsidiary PureTech LLC of $17.2 million as of December 31, 2021, which is related to IPO costs and operating expenses. These intercompany payables do not bear any interest and are repayable upon demand.

6. Profit and loss account

As permitted by Section 408 of the Companies Act 2006, the Parent's profit and loss account has not been included in these financial statements. The Parent's loss for the year was $3.4 million.

7. Directors' remuneration, employee information and share-based payments

The remuneration of the executive Directors of the Parent Company is disclosed in Note 24, Related Parties Transactions, of the accompanying Consolidated Financial Statements. Full details for Directors' remuneration can be found in the Directors' Remuneration Report. Full detail of the share-based payment charge and the related disclosures can be found in Note 8, Share-based Payments, of the accompanying Consolidated Financial Statements.

The Parent had no employees during 2021 or 2020.

History and Development of the Company

We were incorporated and registered under the laws of England and Wales with the Registrar of Companies of England and Wales, United Kingdom in May 2015 as "PureTech Health plc." Our predecessor entity, PureTech Health LLC, or our Predecessor Entity, commenced formal operations and began engaging in initial sourcing activities in 2004, raising its first financing round greater than $5 million in the same year. The Predecessor Entity was acquired by PureTech Health plc on June 18, 2015 in a reorganization completed in connection with our initial public offering on the London Stock Exchange. The Predecessor Entity is now a wholly-owned subsidiary of PureTech Health plc. Our registered office is situated at 8th Floor, 20 Farringdon Street, London EC4A 4AB, United Kingdom, and our telephone number is +(1) 617 482 2333. Our U.S. operations are conducted by our wholly-owned subsidiary PureTech Health LLC, a Delaware limited liability company. Our ordinary shares have traded on the main market of the London Stock Exchange since June 2015 and our ADSs have traded on the Nasdaq Global Market since November 2020. Our agent for service of process in the United States is PureTech Health LLC located at 6 Tide Street, Suite 400, Boston, Massachusetts 02210 where our corporate headquarters and laboratories are located. Our website address is http://puretechhealth.com. The reference to our website is an inactive textual reference only and information contained in, or that can be accessed through, our website or any other website cited in this annual report is not part of hereof.

Risk Factor Annex

Our business faces significant risks. You should carefully consider all of the information set forth in this Annual Report and Accounts, including the following risk factors which we face and which are faced by our industry. These risks are not listed in any particular order of priority and are intended to supplement the risks identified elsewhere. Our business, financial condition or results of operations could be materially and adversely affected if any of these risks occurs.

This Annual Report and Accounts and our associated Annual Report on Form 20-F also contain forward-looking statements that involve risks and uncertainties. Our actual results could differ materially and adversely from those anticipated in these forward-looking statements as a result of certain factors including the risks described below and elsewhere. All statements contained in this Annual Report and Accounts and our associated Annual Report on Form 20-F, other than statements of historical fact, including statements regarding our strategy, future operations, future financial position, future revenues, projected costs, prospects, plans and objectives of management, are forward-looking statements. The words "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "predict," "project," "target," "potential," "would," "could," "should," "continue" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. The forward-looking statements in this Annual Report and Accounts and associated Annual Report on Form 20-F include, among other things, statements about:

- our ability to realize value from our Founded Entities, which may be impacted if we reduce our ownership to a minority interest or otherwise cede control to other investors through contractual agreements or otherwise;
- the success, cost and timing of our clinical development of our Wholly Owned Programs, including the progress of, and results from, our preclinical and clinical trials of LYT-100, LYT-200, LYT-210, LYT-300, LYT-500, LYT-503 /IMB-150, LYT-510, or our therapeutics candidates, and our discovery programs (Alivio, Glyph, Orasome and other technologies, and our meningeal lymphatics discovery research program) and other potential therapeutic candidates within our Wholly Owned Pipeline;
- our ability to obtain and maintain regulatory clearance, authorization, or approval of the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities, and any related restrictions, limitations or warnings in the label of any of the therapeutic candidates, if cleared, authorized, or approved;
- our ability to compete with companies currently marketing or engaged in the development of treatments for indications within our Wholly Owned Pipeline or those of our Founded Entities are designed to target;
- our plans to pursue research and development of other future therapeutic candidates;
- the potential advantages of the therapeutic candidates within our Wholly Owned Pipeline and the therapeutic candidates being developed by our Founded Entities;
- the rate and degree of market acceptance and clinical utility of our therapeutic candidates;
- the success of our collaborations and partnerships with third parties;
- our estimates regarding the potential market opportunity for the therapeutic candidates within our Wholly Owned Pipeline and the therapeutic candidates being developed by our Founded Entities;
- our sales, marketing and distribution capabilities and strategy;
- our ability to establish and maintain arrangements for manufacture of the therapeutic candidates within our Wholly Owned Pipeline and therapeutic candidates being developed by our Founded Entities;
- our intellectual property position;
- our expectations related to the use of capital;
- the effect of the COVID-19 pandemic, including mitigation efforts and economic effects, on any of the foregoing or other aspects of our business operations;
- our estimates regarding expenses, future revenues, capital requirements and needs for additional financing;
- the impact of government laws and regulations; and
- our competitive position.

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. You should refer to the below for a discussion of important factors that may cause our actual results to differ materially from those expressed or implied by our forward-looking statements. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make.

You should read this Annual Report and Accounts, our associated Annual Report on Form 20-F and the documents that we have filed as exhibits to the Annual Report on 20-F completely and with the understanding that our actual future results may be materially different from what we expect. We qualify all of our forward-looking statements by these cautionary statements.

This Annual Report and Accounts and our associated Annual Report on Form 20-F include statistical and other industry and market data that we obtained from industry publications and research, surveys and studies conducted by third parties. Industry publications and third-party research, surveys and studies generally indicate that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information

Risks Related to our Financial Position and Need for Additional Capital

We are a clinical-stage biopharmaceutical company and have incurred significant operating losses since our inception. We may continue to incur significant operating losses for the foreseeable future.

Investment in biotechnology therapeutic development, as well as medical device development, is highly speculative because it entails substantial upfront capital expenditures and significant risk that any potential therapeutic candidate will be unable to demonstrate effectiveness or an acceptable safety profile, gain regulatory approval and become commercially viable. To date, only two of our Founded Entities' therapeutics, Gelesis, Inc.'s Plenity and Akili Interactive Labs, Inc.'s EndeavorRx, have received marketing authorization from the U.S. Food and Drug Administration, or the FDA, and marketing authorization granted in the European Economic Area, or EEA, and in other countries that recognize the CE Mark, or CE Mark market authorizations. All of the therapeutic candidates in our Wholly Owned Pipeline and the majority of our Founded Entities' therapeutic candidates may require substantial additional development time, including extensive clinical research, and resources before we would be able to apply for or receive regulatory clearances or approvals and begin generating revenue from therapeutic sales.

Since our inception, we have invested most of our resources in developing our technology and therapeutic candidates, building our intellectual property portfolio, developing our supply chain, conducting business planning, raising capital and providing general and administrative support for these operations, including with respect to our Founded Entities. We are not operationally profitable and have incurred operating losses in each year since our inception. Our operating losses for the years ended December 31, 2019, 2020 and 2021 were $135.4 million, $119.6 million, and $149.2 million, respectively. We have no therapeutics developed in our Wholly Owned Pipeline approved for commercial sale and have not generated any revenues from therapeutic sales, and we and our Founded Entities have financed operations solely through the sale of equity securities, revenue from strategic alliances and government funding and, with respect to certain of our Founded Entities, debt financings. We continue to incur significant research and development, or R&D, and other expenses related to ongoing operations and expect to incur losses for the foreseeable future. We anticipate continued losses for the foreseeable future.

Due to risks and uncertainties associated with the development of drugs, biologics and medical devices, we are unable to predict the timing or amount of our expenses, or when we will be able to generate any meaningful revenue or achieve or maintain profitability, if ever. In addition, our expenses could increase beyond our current expectations if we are required by the FDA, the European Medicines Agency, or the EMA, or other comparable foreign regulatory authorities to perform preclinical studies or clinical trials in addition to those that we currently anticipate, or if there are any delays in any of our or our future collaborators' clinical trials or the development of our existing therapeutic candidates and any other therapeutic candidates that we may identify. Even if our existing therapeutic candidates or any future therapeutic candidates that we may identify are approved for commercial sale, we anticipate incurring significant costs associated with commercializing any approved therapeutic and ongoing compliance efforts.

As of December 31, 2021, we had never generated revenue from the therapeutic candidates within our Wholly Owned Pipeline, and we may never be operationally profitable.

While Gelesis, Inc., or Gelesis, and Akili Interactive Labs, Inc., or Akili, have received marketing authorization for Plenity and EndeavorRx, respectively, from the FDA and CE Mark market authorizations, we may never be able to develop or commercialize marketable therapeutics or achieve operational profitability. Revenue from the sale of any therapeutic candidate for which regulatory clearance, authorization or approval is obtained will be dependent, in part, upon the size of the markets in the territories for which we gain regulatory clearance, authorization or approval, the accepted price for the therapeutic, the ability to obtain reimbursement at any price and whether we own the commercial rights for that territory. Our growth strategy depends on our ability to generate revenue. In addition, if the

number of addressable patients is not as anticipated, the indication or intended use cleared, authorized or approved by regulatory authorities is narrower than expected, or the reasonably accepted population for treatment is narrowed by competition, physician choice or treatment guidelines, we may not generate significant revenue from sales of such therapeutics, even if cleared, authorized or approved. Even if we are able to generate revenue from the sale of any cleared, authorized or approved therapeutics, we may not become operationally profitable and may need to obtain additional funding to continue operations. Even if we achieve operational profitability in the future, we may not be able to sustain profitability in subsequent periods.

If we are unable to achieve sustained profitability, it would depress the value of our company and could impair our ability to raise capital, expand our business, diversify our R&D pipeline, market the therapeutic candidates within our Wholly Owned Pipeline, if cleared or approved, and pursue or continue our operations. Our prior losses, combined with expected future losses, have had and may continue to have an adverse effect on our shareholders' equity and working capital.

We may require substantial additional funding to achieve our business goals. If we are unable to obtain this funding when needed and on acceptable terms, we could be forced to delay, limit or terminate certain of our therapeutic development efforts. Certain of our Founded Entities will similarly require substantial additional funding to achieve their business goals.

Across the entire portfolio, we established the underlying programs and platforms that have resulted in 27 therapeutics and therapeutic candidates that are being advanced within our Wholly Owned Programs or by our Founded Entities. Of these therapeutics and therapeutic candidates, 16 are clinical-stage and two have been authorized for marketing by the FDA and granted CE Mark marketing authorizations. Developing biopharmaceutical therapeutics is expensive and time-consuming, and with respect to the therapeutic candidates within our Wholly Owned Pipeline, we expect to require substantial additional capital to conduct research, preclinical studies and clinical trials for our current and future programs, establish pilot scale and commercial scale manufacturing processes and facilities, seek regulatory approvals for the therapeutic candidates within our Wholly Owned Pipeline and launch and commercialize any therapeutics for which we receive regulatory approval, including building our own commercial sales, marketing and distribution organization. With respect to our Founded Entities' programs, we anticipate that we will continue to fund a small portion of development costs by strategically participating in such companies' financings when doing so would be in the interests of our shareholders. The form of any such participation may include investment in public or private financings, collaboration and partnership arrangements and licensing arrangements, among others. Our management and strategic decision makers have not made decisions regarding the future allocation of certain of our resources among our Founded Entities, but evaluate the needs and opportunities with respect to each of these Founded Entities routinely and on a case-by-case basis. In connection with any collaboration agreements relating to our Wholly Owned Programs, we are also responsible for the payments to third parties of expenses that may include milestone payments, license maintenance fees and royalties, including in the case of certain of our agreements with academic institutions or other companies from whom intellectual property rights underlying their respective programs have been in-licensed or acquired. Because the outcome of any preclinical or clinical development and regulatory approval process is highly uncertain, we cannot reasonably estimate the actual amounts necessary to successfully complete the development, regulatory approval process and potential commercialization of our Wholly Owned Programs and any future therapeutic candidates we may identify.

As of December 31, 2021, we had cash and cash equivalents of $465.7 million at the PureTech Health plc level. However, our operating plan may change as a result of many factors currently unknown to us, and we may need to seek additional funds sooner than planned, through public or private equity or debt financings, sales of assets or programs, other sources, such as strategic collaborations or license and development agreements, or a combination of these approaches. Even if we believe we have sufficient funds for our current or future operating plans, we may opportunistically seek additional capital if market conditions are favorable or if we have specific strategic considerations. Our spending will vary based on new and ongoing therapeutic development and corporate activities. Any such additional fundraising efforts for us may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize therapeutic candidates that we may identify and pursue. Moreover, such financing may result in dilution to shareholders, imposition of debt covenants and repayment obligations, or other restrictions that may affect our business.

Our future funding requirements, both short-term and long-term, will depend on many factors, including, but not limited to:

- the time and cost necessary to complete ongoing, planned and future unplanned clinical trials, including our ongoing clinical trials for certain of our therapeutic candidates, and potential future clinical trials for certain of our therapeutic candidates;
- the outcome, timing and cost of meeting regulatory requirements established by the FDA, the EMA and other comparable foreign regulatory authorities;
- the progress, timing, scope and costs of our preclinical studies, clinical trials and other related activities for our ongoing and planned clinical trials, and potential future clinical trials;
- the costs of obtaining clinical and commercial supplies of raw materials and drug products for the therapeutic candidates within our Wholly Owned Pipeline, as applicable, and any other therapeutic candidates we may identify and develop;
- our ability to successfully identify and negotiate acceptable terms for third-party supply and contract manufacturing agreements with contract manufacturing organizations, or CMOs;
- the costs of commercialization activities for any of the therapeutic candidates within our Wholly Owned Pipeline that receive marketing approval, including the costs and timing of establishing therapeutic sales, marketing, distribution and manufacturing capabilities, or entering into strategic collaborations with third parties to leverage or access these capabilities;
- the amount and timing of sales and other revenues from the therapeutic candidates within our Wholly Owned Pipeline, if approved, including the sales price and the availability of coverage and adequate third-party reimbursement;
- the cash requirements of our Founded Entities and our ability and willingness to provide them with financing;
- the cash requirements of any future acquisitions or discovery of therapeutic candidates;
- the time and cost necessary to respond to technological and market developments, including other therapeutics that may compete with one or more of our Wholly Owned Programs;
- the costs of acquiring, licensing or investing in intellectual property rights, therapeutics, therapeutic candidates and businesses;
- our ability to attract, hire and retain qualified personnel as we expand R&D and establish a commercial infrastructure;
- the costs of maintaining, expanding and protecting our intellectual property portfolio; and
- the costs of operating as a public company in the United Kingdom and the United States and maintaining listings on both the London Stock Exchange, or the LSE, and The Nasdaq Global Market, or Nasdaq.

We cannot be certain that additional funding will be available on acceptable terms, or at all. If adequate funds are not available to us on a timely basis, we may be required to delay, limit or terminate one or more research or development programs or the potential commercialization of any approved therapeutics or be unable to expand operations or otherwise capitalize on business opportunities, as desired, which could materially affect our business, prospects, financial condition and results of operations.

Raising additional capital may cause dilution to our existing shareholders, restrict our operations or require us to relinquish rights to current therapeutic candidates or to any future therapeutic candidates on unfavorable terms.

We expect our expenses to increase in connection with our planned operations. Unless and until we can generate a substantial amount of revenue from the therapeutic candidates within our Wholly Owned Pipeline or royalties and other monetization events related to our Founded Entities, we expect to finance our future cash needs through a combination of public and private equity offerings, debt financings, strategic partnerships, sales of assets and alliances and licensing arrangements. We, and indirectly, our shareholders, may bear the cost of issuing and servicing any such securities and of entering into and maintaining any such strategic partnerships or other arrangements. Because any decision by us to issue debt or equity securities in the future will depend on market conditions and other factors beyond our control, we cannot predict or estimate the amount, timing or nature of any future financing transactions. To the extent that we or our Founded Entities raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms may include liquidation or other preferences that adversely affect your rights as a shareholder. The incurrence of additional indebtedness would result in increased fixed payment obligations and could involve additional restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. Additionally, any future collaborations we enter into with third parties may provide capital in the near term, but limit our potential cash flow and revenue in the future.

If we raise additional funds through strategic partnerships and alliances and licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies or therapeutic candidates, or grant licenses or other rights on unfavorable terms.

In addition, if any of our Founded Entities raises funds through the issuance of equity securities, our shareholders' indirect equity interest in such Founded Entity could be substantially diminished. If any of our Founded Entities raises additional funds through collaboration and licensing arrangements, it may be necessary to relinquish some rights to our technologies or these therapeutic candidates or grant licenses on terms that are not favorable to us.

If we engage in acquisitions or strategic partnerships, this may increase our capital requirements, dilute our shareholders, cause us to incur debt or assume contingent liabilities and subject us to other risks.

We may engage in various acquisitions and strategic partnerships in the future, including licensing or acquiring complementary therapeutics, intellectual property rights, technologies or businesses. Any acquisition or strategic partnership may entail numerous risks, including:

- increased operating expenses and cash requirements;
- the assumption of indebtedness or contingent liabilities;
- the issuance of our equity securities which would result in dilution to our shareholders;
- assimilation of operations, intellectual property, therapeutics and therapeutic candidates of an acquired company, including difficulties associated with integrating new personnel;
- the diversion of our management's attention from our existing therapeutic programs and initiatives in pursuing such an acquisition or strategic partnership;
- retention of key employees, the loss of key personnel and uncertainties in our ability to maintain key business relationships;
- risks and uncertainties associated with the other party to such a transaction, including the prospects of that party and their existing therapeutics or therapeutic candidates and regulatory approvals; and
- our inability to generate revenue from acquired intellectual property, technology and/or therapeutics sufficient to meet our objectives or even to offset the associated transaction and maintenance costs.

In addition, if we undertake such a transaction, we may issue dilutive securities, assume or incur debt obligations, incur large one-time expenses and acquire intangible assets that could result in significant future amortization expense.

Risks Related to Our Founded Entities

Our ability to realize value from our Founded Entities may be impacted if we reduce our ownership or otherwise cede control to other investors through contractual agreements or otherwise.

We do not have a majority interest in our Non-Controlled Founded Entities. Our interests may be further reduced as such companies raise capital from third-party investors. In addition, we may agree to contractual arrangements for the funding of further developments by one or more of our Founded Entities. As a result, with respect to our Non-Controlled Founded Entities, we may not be able to exercise control over the affairs of such Founded Entity, including that Founded Entity's governance arrangements and access to management and financial information. We are also party to agreements with certain of our Founded Entities that contain provisions which could force us to exit from that Founded Entity at a time and/or price determined by other investor(s) (for example, by the exercise of drag-along rights). If we were forced to exit out of a Founded Entity, this could have a material adverse effect on our business, financial condition or results of operations and prospects. In addition, if the affairs of one or more Founded Entities in which we hold a minority stake were to be conducted in a manner detrimental to our interests or intentions, our business, reputation and prospects may be adversely affected.

As certain of our Founded Entities have completed equity financings, they have entered into certain agreements with the investors participating in such financings, including us. We are party to voting agreements with Entrega, Inc., or Entrega, Sonde Health, Inc., or Sonde, Vedanta Biosciences, Inc., or Vedanta, and Follica, Incorporated, or Follica; investors' rights agreements with Akili, Follica, Vedanta, Entrega, Sonde and Vor Biopharma Inc., or Vor, and stockholders' agreements with Gelesis, Akili, Follica, Vedanta, Entrega, and Sonde, pursuant to which we are subject to certain restrictions on the transfer or sale of shares (e.g., pre-emptive rights or drag-along, tag-along rights or lock up agreements), and we may not be able freely to transfer our interest in such Founded Entities or procure the sale of the entire issued share capital of such Founded Entities, similar to other investors who are party to these agreements. In addition, many of our Founded Entities have employee share plans which further dilute our interest in such business. If the affairs of one or more of our Founded Entities were to be conducted in a manner detrimental to our interests or intentions or if we were unable to realize our interest in a Founded Entity or suffer dilution of our shareholding, this could have a material adverse effect on our business, financial condition or results of operation and prospects.

Our overall value may be dominated by a single or limited number of our Founded Entities.

A large proportion of our overall value may at any time reside in a small proportion of our Founded Entities. Accordingly, there is a risk that if one or more of the intellectual property or commercial rights relevant to a valuable business were impaired, this would have a material adverse impact on our overall value. Furthermore, a large proportion of our overall revenue may at any time be the subject of one, or a small number of, licensed technologies. Should the relevant licenses be terminated or expire this would be likely to have a material adverse effect on the revenue received by us. Any material adverse impact on the value of the business of a Founded Entity could, in the situations described above, or otherwise, have a material adverse effect on our business, financial condition, trading performance and/or prospects.

We have limited information about and limited control or influence over our Non-Controlled Founded Entities.

While we maintain ownership of equity interests in our Non-Controlled Founded Entities, we do not maintain voting control or direct management and development efforts for these entities. Each of these entities are independently managed, and we do not control the clinical and regulatory development of these Non-Controlled Founded Entities' therapeutic candidates. Any failure by our Non-Controlled Founded Entities to adhere to regulatory requirements, initiate preclinical studies and clinical trials on schedule or to obtain clearances or approvals for their therapeutic candidates could have an adverse effect on our business, financial condition, results of operation and prospects. The information included in this report about our Non-Controlled Founded Entities is based on (i) our knowledge, which may in some cases be limited, (ii) information that is publicly available, including the public filings of SEC reporting companies, such as Karuna, Vor and Gelesis, and (iii) information provided to us by our Non-Controlled Founded Entities. Where a date is provided, the information included in this report about our Non-Controlled Founded Entities is as of that date and you should not assume that it is accurate as of any other date. As such, there may be developments at our Non-Controlled Founded Entities of which we are unaware that could have an adverse effect on our business, financial condition, results of operation and prospects.

Our Founded Entities are difficult to value given that many of their therapeutic candidates are in the development stage.

Investments in early-stage companies, particularly privately held entities, are inherently difficult to value since sales, cash flow and tangible asset values are very limited, which makes the valuation highly dependent on expectations of future development, and any future significant revenues would only arise in the medium to longer terms and are uncertain. Equally, investments in companies just commencing the commercial stage are also difficult to value since sales, cash flow and tangible assets are limited, they have only commenced initial receipts of revenues and valuations are still dependent on expectations of future development. There can be no guarantee that our valuation of our Founded Entities will be considered to be correct in light of the early stage of development for many of these entities and their future performance. As a result, we may not realize the full value of our ownership in such Founded Entities which could adversely affect our business and results of operations. For example, on November 15, 2019, resTORbio, Inc., or resTORbio, announced that its lead therapeutic candidate, RTB101, did not meet its primary endpoint in its Phase 3 study and ceased further development leading to a decline in resTORbio's stock price from $9.27 to $1.09 and our sale of 7,680,700 common shares of resTORbio. As a result of the foregoing, we recognized a total cash loss of approximately $10 million from our initial investment through sale of shares.

Certain of our and our Founded Entities' therapeutics and therapeutic candidates represent novel therapeutic approaches and negative perception of any therapeutic or therapeutic candidate that we or they develop could adversely affect our ability to conduct our business, obtain and maintain regulatory clearance, authorization or approvals or identify alternate regulatory pathways to market for such therapeutic candidate.

Certain of our and our Founded Entities' therapeutic candidates are considered relatively new and novel therapeutic approaches. Our and their success will depend upon physicians who specialize in the treatment of diseases targeted by our and their therapeutic candidates, prescribing potential treatments that involve the use of our and their therapeutic candidates, if approved, in lieu of, or in addition to, existing treatments with which they are more familiar and for which greater clinical data may be available. Access will also depend on consumer acceptance and adoption of therapeutics that are commercialized. In addition, responses by the U.S., state or foreign governments to negative public perception or ethical concerns may result in new legislation or regulations that could limit our or our Founded Entities' ability to develop or commercialize any

therapeutic candidates, obtain or maintain regulatory approval, identify alternate regulatory pathways to market or otherwise achieve profitability. More restrictive statutory regimes, government regulations or negative public opinion would have an adverse effect on our business, financial condition, results of operations and prospects and may delay or impair the development and commercialization of our or our Founded Entities' therapeutic candidates or demand for any therapeutics we or they may develop.

For example, in the United States and the European Union, no therapeutics to date have been approved specifically demonstrating an impact on the microbiome as part of their therapeutic effect. Vedanta is developing a pipeline of microbiome-derived modulators for immune and infectious disease. Microbiome therapies may not be successfully developed or commercialized or gain the acceptance of the public or the medical community. Additionally, adverse events, or AEs, in non-investigational new drug application, or IND, human clinical studies and clinical trials of Vedanta's therapeutic candidates or in clinical trials of other companies developing similar therapeutics and the resulting publicity, similarly to the AEs publicized with respect to Seres Therapeutics, Inc.'s SER-287 Phase 2 clinical trial, as well as any other AEs in the field of the microbiome, could result in a decrease in demand for any therapeutic that Vedanta may develop. Finally, the FDA, the EMA or other comparable foreign regulatory authorities may lack experience in evaluating the safety and efficacy of therapeutic candidates based on microbiome therapeutics, which could result in a longer than expected regulatory review process, increase expected development costs and delay or prevent potential commercialization of therapeutic candidates.

Risks Related to the Clinical Development, Regulatory Review and Approval of our and our Founded Entities' Therapeutic Candidates

Risks Related to Clinical Development

The therapeutic candidates within our Wholly Owned Pipeline and most of our Founded Entities' therapeutic candidates are in preclinical or clinical development, which is a lengthy and expensive process with uncertain outcomes and the potential for substantial delays. We cannot give any assurance that any of our and our Founded Entities' therapeutic candidates will receive regulatory clearance, authorization or approval, which is necessary before they can be commercialized.

Before obtaining marketing clearance, authorization or approval from regulatory authorities for the sale of our or our Founded Entities' therapeutic candidates, we or our Founded Entities must conduct extensive clinical trials to demonstrate the safety and efficacy, or with respect to biologics, safety, purity and potency, of the therapeutic candidates in humans. To date, we have focused substantially all of our efforts and financial resources on identifying, acquiring, and developing therapeutic candidates, including conducting lead optimization, preclinical studies and clinical trials, and providing general and administrative support for these operations. To date, only two of our Founded Entities' therapeutic candidates, Gelesis' Plenity and Akili's EndeavorRx, have received marketing authorization from the FDA, and we cannot be certain that any of our internal or our Founded Entities' other therapeutic candidates will receive regulatory clearance, authorization or approval, the timing of such clearance, authorization or approval, if received, or that clinical trials will progress as planned. Our or our Founded Entities' inability to successfully complete preclinical and clinical development could result in additional costs to us and negatively impact our ability to generate revenue. Our future success is dependent on our and our Founded Entities' ability to successfully develop, obtain regulatory clearance, authorization or approval for, and then successfully commercialize therapeutic candidates. We and our Founded Entities, with the exceptions of Gelesis and Akili, currently have no drugs or biologics approved or devices cleared, authorized or approved for sale and have not generated any revenue from sales of drugs, biologics or devices. We cannot guarantee that we or our Founded Entities will be able in the future to develop or successfully commercialize any of our or their therapeutic candidates. Additionally, there is currently no FDA approved live biological therapeutic using a defined cocktail of microbes, which could result in regulatory complexity in Vedanta's pipeline. There is also no approved drug therapy for lymphedema, which will require us to engage In further discussions with the FDA on requirements for potential approval.

Other than Gelesis' Plenity and Akili's EndeavorRx, all of our Wholly Owned Programs and our Founded Entities' therapeutic candidates require additional development; management of preclinical, clinical, and manufacturing activities; and/or regulatory clearances, authorization or approvals. In addition, we or our Founded Entities may need to obtain adequate manufacturing supply; build a commercial organization; commence marketing efforts; and obtain coverage and reimbursement before we generate any significant revenue from commercial therapeutic sales, if ever. Many of the therapeutic candidates in our Wholly Owned Pipeline and our Founded Entities' therapeutic candidates are in early-stage research or translational phases of development, and the risk of failure for these programs is high. We cannot be certain that any of the therapeutic candidates in our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates will be successful in clinical trials or receive regulatory approval, authorization or clearance. Further, our Wholly Owned Programs or our Founded Entities' therapeutic candidates may not receive regulatory clearance, authorization or approval even if we believe they are successful in clinical trials. If we or our Founded Entities do not receive regulatory clearance, authorization or approval for our or their therapeutic candidates, we may not be able to continue operations, which may result in dissolution, out-licensing the technology or pursuing an alternative strategy.

Preclinical development is uncertain. Our preclinical programs may experience delays or may never advance to clinical trials, which would adversely affect our ability to obtain regulatory clearance, authorization or approvals or commercialize these programs on a timely basis or at all, which would have an adverse effect on our business.

Certain of our Wholly Owned Programs are in the preclinical stage, and their risk of failure is high. Before we can commence clinical trials for a therapeutic candidate, we must complete extensive preclinical testing and studies that support our planned INDs, in the United States, or similar applications in other jurisdictions. We cannot be certain of the timely completion or outcome of our preclinical testing and studies and cannot predict if the FDA or other regulatory authorities will accept our proposed clinical programs or if the outcome of our preclinical testing and studies will ultimately support the further development of our programs. As a result, we cannot be sure that we will be able to submit INDs or similar applications for our preclinical programs on the timelines we expect, if at all, and we cannot be sure that submission of INDs or similar applications will result in the FDA, the EMA or other regulatory authorities allowing clinical trials to begin.

Clinical trials of our or our Founded Entities' therapeutic candidates may be delayed, and certain programs may never advance in the clinic or may be more costly to conduct than we anticipate, any of which can affect our ability to fund our company and would have a material adverse impact on our platform or our business.

Clinical testing is expensive, time-consuming, and subject to uncertainty. We cannot guarantee that any of our ongoing and planned clinical trials will be conducted as planned or completed on schedule, if at all. Moreover, even if these trials are initiated or conducted on a timely basis, issues may arise that could result in the suspension or termination of such clinical trials. A failure of one or more clinical trials can occur at any stage of testing, and our clinical trials may not be successful. Events that may prevent successful or timely initiation or completion of clinical trials include:

- inability to generate sufficient preclinical, toxicology, or other in vivo or in vitro data to support the initiation or continuation of clinical trials;
- delays in confirming target engagement, patient selection or other relevant biomarkers to be utilized in preclinical and clinical therapeutic candidate development;
- delays in reaching a consensus with regulatory agencies as to the design or implementation of our clinical studies;
- delays in reaching agreement on acceptable terms with prospective contract research organizations, or CROs, and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and clinical trial sites;
- delays in identifying, recruiting and training suitable clinical investigators;
- delays in obtaining required Institutional Review Board, or IRB, approval at each clinical trial site;
- imposition of a temporary or permanent clinical hold by regulatory agencies for a number of reasons, including after review of an IND or amendment, clinical trial application, or CTA, or amendment, investigational device exemption, or IDE, or supplement, or equivalent application or amendment; as a result of a new safety finding that presents unreasonable risk to clinical trial participants; or a negative finding from an inspection of our clinical trial operations or study sites;
- developments in trials for other therapeutic candidates with the same targets or related modalities as our or our Founded Entities' therapeutic candidates conducted by competitors that raise regulatory or safety concerns about risk to patients of the treatment, or if the FDA finds that the investigational protocol or plan is clearly deficient to meet its stated objectives;
- difficulties in securing access to materials for the comparator arm of certain of our clinical trials;
- delays in identifying, recruiting and enrolling suitable patients to participate in clinical trials, and delays caused by patients withdrawing from clinical trials or failing to return for post-treatment follow-up;
- difficulties in finding a sufficient number of trial sites, or trial sites deviating from trial protocol or dropping out of a trial;
- difficulty collaborating with patient groups and investigators;

- failure by CROs, other third parties, or us to adhere to clinical trial requirements;
- failure by CROs, other third parties, or us to perform in accordance with the FDA's or any other regulatory authority's current good clinical practices, or GCP, requirements, or regulatory guidelines in other countries;
- occurrence of AEs or undesirable side effects or other unexpected characteristics associated with the therapeutic candidate that are viewed to outweigh its potential benefits;
- changes in regulatory requirements and guidance that require amending or submitting new clinical protocols;
- changes in the standard of care on which a clinical development plan was based, which may require new or additional trials;
- the cost of clinical trials of any therapeutic candidates that we may identify and pursue being greater than we anticipate;
- clinical trials of any therapeutic candidates that we may identify and pursue producing negative or inconclusive results, which may result in our deciding, or regulators requiring us, to conduct additional clinical trials or abandon therapeutic development programs;
- transfer of manufacturing processes to larger-scale facilities operated by a CMO, or by us, and delays or failures by our CMOs or us to make any necessary changes to such manufacturing process;
- delays in manufacturing, testing, releasing, validating, or importing/exporting sufficient stable quantities of therapeutic candidates that we may identify for use in clinical trials or the inability to do any of the foregoing; and
- factors we may not be able to control, such as current or potential pandemics or other events that may limit patients, principal investigators or staff or clinical site availability, result in clinical trial protocol deviations, or impact supply of our or our Founded Entities' therapeutic candidates (e.g., the COVID-19 pandemic or the developing conflict between Russia and Ukraine).

Any inability to successfully initiate or complete clinical trials could result in additional costs to us or impair our ability to generate revenue. In addition, if we make manufacturing or formulation changes to our Wholly Owned Programs, we may be required to or we may elect to conduct additional preclinical studies or clinical trials to bridge data obtained from our modified therapeutic candidates to data obtained from preclinical and clinical research conducted using earlier versions. Clinical trial delays could also shorten any periods during which our therapeutics have patent protection and may allow our competitors to bring therapeutics to market before we do, which could impair our ability to successfully commercialize therapeutic candidates and may harm our business and results of operations.

We could also encounter delays if a clinical trial is suspended or terminated by us, by the data safety monitoring board, or DSMB, or by the FDA, the EMA or other comparable foreign regulatory authorities, or if the IRBs of the institutions in which such trials are being conducted suspend or terminate the participation of their clinical investigators and sites subject to their review. Such authorities may suspend or terminate a clinical trial due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA, the EMA or other comparable foreign regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a therapeutic candidate, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial.

Moreover, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and receive compensation in connection with such services. Under certain circumstances, we may be required to report some of these relationships to the FDA, the EMA or comparable foreign regulatory authorities. The FDA, the EMA or comparable foreign regulatory authority may conclude that a financial relationship between us and a principal investigator has created a conflict of interest or otherwise affected interpretation of the study. The FDA, the EMA or comparable foreign regulatory authority may therefore question the integrity of the data generated at the applicable clinical trial site and the utility of the clinical trial itself may be jeopardized. This could result in a delay in approval, or rejection, of our marketing applications by the FDA, the EMA or comparable foreign regulatory authority, as the case may be, and may ultimately lead to the denial of marketing approval of one or more of our Wholly Owned Programs or our Founded Entities' therapeutic candidates.

Delays in the initiation, conduct or completion of any clinical trial of the therapeutic candidates within our Wholly Owned Pipeline will increase our costs, slow down the therapeutic candidate development and approval process and delay or potentially jeopardize our ability to commence therapeutic sales and generate revenue. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates. In the event we identify any additional therapeutic candidates to pursue, we cannot be sure that submission of an IDE, IND, CTA, or equivalent application, as applicable, will result in the FDA, the EMA or comparable foreign regulatory authority allowing clinical trials to begin in a timely manner, if at all. Any of these events could have a material adverse effect on our business, prospects, financial condition and results of operations.

The results of early-stage clinical trials and preclinical studies may not be predictive of future results. Initial data in clinical trials may not be indicative of results obtained when these trials are completed or in later stage trials.

The results of preclinical studies may not be predictive of the results of clinical trials, and the results of any early-stage clinical trials we commence may not be predictive of the results of the later-stage clinical trials. The results of preclinical studies and clinical trials in one set of patients or disease indications, or from preclinical studies or clinical trials that we did not lead, may not be predictive of those obtained in another. In some instances, there can be significant variability in safety or efficacy results between different clinical trials of the same therapeutic candidate due to numerous factors, including changes in trial procedures set forth in protocols, differences in the size and type of the patient populations, changes in and adherence to the dosing regimen and other clinical trial protocols and the rate of dropout among clinical trial participants. In addition, preclinical and clinical data are often susceptible to various interpretations and analyses, and many companies that have believed their therapeutic candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval. A number of companies in the pharmaceutical, biopharmaceutical and biotechnology industries have suffered significant setbacks in clinical development even after achieving promising results in earlier studies, and any such setbacks in our clinical development could have a material adverse effect on our business and operating results. Even if early-stage clinical trials are successful, we may need to conduct additional clinical trials of our Wholly Owned Programs in additional patient populations or under different treatment conditions before we are able to seek approvals or clearances from the FDA, the EMA or other comparable foreign regulatory authorities to market and sell these therapeutic candidates. Our failure to obtain marketing authorization for the therapeutic candidates within our Wholly Owned Pipeline would substantially harm our business, prospects, financial condition and results of operations.

If we encounter difficulties enrolling patients in clinical trials, our clinical development activities could be delayed or otherwise adversely affected.

Identifying and qualifying trial participants to participate in clinical studies is critical to our success. The timing of our clinical studies depends on the speed at which we can recruit trial participants to participate in testing the therapeutic candidates within our Wholly Owned Pipeline. Delays in enrollment may result in increased costs or may affect the timing or outcome of the planned clinical trials, which could prevent completion of these trials and adversely affect our ability to advance the development of the therapeutic candidates within our Wholly Owned Pipeline. If trial participants are unwilling to participate in our studies because of negative publicity from AEs in our trials or other trials of similar therapeutics, or those related to specific therapeutic area, or for other reasons, including competitive clinical studies for similar patient populations, the timeline for recruiting trial participants, conducting studies, and obtaining regulatory approval of potential therapeutics may be delayed. We also may face delays as a result of unforeseen global circumstances, for example we have experienced temporary delays in certain of our clinical development activities, including enrolling participants in certain of our clinical trials, as a result of the COVID-19 pandemic or the developing conflict between Russia and Ukraine. Any delays could result in increased costs, delays in advancing our therapeutic candidate development, delays in testing the effectiveness of the therapeutic candidates within our Wholly Owned Pipeline, or termination of the clinical studies altogether.

We may not be able to identify, recruit and enroll a sufficient number of trial participants, or those with required or desired characteristics to achieve diversity in a study, to complete our clinical studies in a timely manner. Patient and subject enrollment is affected by factors including:

- the size and nature of a patient population;
- the patient eligibility criteria defined in the applicable clinical trial protocols, which may limit the patient populations eligible for clinical trials to a greater extent than competing clinical trials for the same indication;
- the size of the study population required for analysis of the trial's primary endpoints;
- the severity of the disease under investigation;
- the proximity of patients to a trial site;
- the inclusion and exclusion criteria for the trial in question;

- the design of the trial protocol;
- the ability to recruit clinical trial investigators with the appropriate competencies and experience;
- the availability and efficacy of approved medications or therapies for the disease or condition under investigation;
- clinicians' and patients' perceptions as to the potential advantages and side effects of the therapeutic candidate being studied in relation to other available therapies and therapeutic candidates;
- the ability to obtain and maintain patient consents; and
- the risk that patients enrolled in clinical trials will not complete such trials, for any reason.

Furthermore, our or our collaborators' ability to successfully initiate, enroll and conduct a clinical trial outside the United States is subject to numerous additional risks, including:

- difficulty in establishing or managing relationships with CROs and physicians;
- differing standards for the conduct of clinical trials;
- differing standards of care for patients with a particular disease;
- an inability to locate qualified local consultants, physicians and partners; and
- the potential burden of complying with a variety of foreign laws, medical standards and regulatory requirements, including the regulation of pharmaceutical and biotechnology therapeutics and treatments.

If we have difficulty enrolling sufficient numbers of patients to conduct clinical trials as planned, we may need to delay or terminate clinical trials, either of which would have an adverse effect on our business.

Use of the therapeutic candidates within our Wholly Owned Pipeline or the therapeutic candidates being developed by our Founded Entities could be associated with side effects, AEs or other properties or safety risks, which could delay or halt their clinical development, prevent their regulatory clearance, authorization or approval, cause us to suspend or discontinue clinical trials, abandon a therapeutic candidate, limit their commercial potential, if cleared, authorized or approved, or result in other significant negative consequences that could severely harm our business, prospects, operating results and financial condition.

As is the case with pharmaceuticals generally, it is likely that there may be side effects and AEs associated with our and our Founded Entities' drug or biologic therapeutic candidates' use. Similarly, investigational devices may also be subject to side effects and AEs. Results of our clinical trials or those being conducted by Founded Entities could reveal a high and unacceptable severity and prevalence of side effects or unexpected characteristics. Undesirable side effects caused by these therapeutic candidates could cause us, our Founded Entities or regulatory authorities to interrupt, delay or halt clinical trials and could result in more restrictive labeling or the delay or denial of regulatory clearance, authorization or approval by the FDA, the EMA or other comparable foreign regulatory authorities. The side effects related to the therapeutic candidate could affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. Any of these occurrences may harm our business, financial condition and prospects significantly.

Moreover, if therapeutic candidates within our Wholly Owned Pipeline are associated with undesirable side effects in preclinical studies or clinical trials or have characteristics that are unexpected, we may elect to abandon their development or limit their development to more narrow uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective, which may limit the commercial expectations for the therapeutic candidate if approved. We may also be required to modify or terminate our study plans based on findings in our preclinical studies or clinical trials. Many therapeutic candidates that initially show promise in early-stage testing may later be found to cause side effects that prevent further development. As we work to advance existing therapeutic candidates and to identify new therapeutic candidates, we cannot be certain that later testing or trials of therapeutic candidates that initially showed promise in early testing will not be found to cause similar or different unacceptable side effects that prevent their further development.

It is possible that as we test the therapeutic candidates within our Wholly Owned Pipeline in larger, longer and more extensive clinical trials, or as the use of these therapeutic candidates becomes more widespread if they receive regulatory clearance or approval, illnesses, injuries, discomforts and other AEs that were observed in earlier trials, as well as conditions that did not occur or went undetected in previous trials, will be reported by subjects. If such side effects become known later in development or upon approval, if any, such findings may harm our business, financial condition and prospects significantly. Additionally, adverse developments in clinical trials of pharmaceutical, biopharmaceutical or biotechnology therapeutics conducted by others may cause the FDA or other regulatory oversight bodies to suspend or terminate our clinical trials or to change the requirements for approval of any of our Wholly Owned Programs.

In addition to side effects caused by the therapeutic candidate, the administration process or related procedures also can cause adverse side effects. If any such AEs occur, our clinical trials could be suspended or terminated. If we are unable to demonstrate that any AEs were not caused by therapeutic candidate, the FDA, the European Commission, the EMA, or other regulatory authorities could order us to cease further development of, or deny clearance or approval of, a therapeutic candidate for any or all targeted indications. Even if we can demonstrate that all future serious adverse events, or SAEs, are not therapeutic-related, such occurrences could affect patient recruitment or the ability of enrolled patients to complete the trial. Moreover, if we elect, or are required, to not initiate, delay, suspend or terminate any future clinical trial of any of our Wholly Owned Programs, the commercial prospects of such therapeutic candidates may be harmed and our ability to generate therapeutic revenues from any of these therapeutic candidates may be delayed or eliminated. Any of these occurrences may harm our ability to develop other therapeutic candidates, and may harm our business, financial condition and prospects significantly.

Additionally, if any of the therapeutic candidates within our Wholly Owned Pipeline receives marketing authorization, the FDA could impose contraindications or a boxed warning in the labeling of our therapeutic. For any of our drug or biologic therapeutic candidates receiving marketing authorization, the FDA could require us to adopt a risk evaluation and mitigation strategy, or REMS, and could apply elements to assure safe use to ensure that the benefits of the therapeutic outweigh its risks, which may include, among other things, a Medication Guide outlining the risks of the therapeutic for distribution to patients, a requirement that clinicians or health care settings to become certified prior to prescribing and to participate in additional REMS activities, such as training, patient counseling, and monitoring, and a communication plan to health care practitioners. Furthermore, if we or others later identify undesirable side effects caused by the therapeutic candidates within our Wholly Owned Pipeline once approved, several potentially significant negative consequences could result, including:

- regulatory authorities may suspend or withdraw approvals of such therapeutic candidate, or seek an injunction against its manufacture or distribution;
- regulatory authorities may require additional warnings in the labeling, including boxed warnings, or issue safety alerts, Dear Healthcare Provider letters, press releases or other communications containing warnings or other safety information about the therapeutic;
- we may be required by the FDA to implement a REMS for a marketed drug or biologic;
- we may be required to change the way a therapeutic candidate is administered or conduct additional clinical trials;
- we may be subject to fines, injunctions or the imposition of civil or criminal penalties;
- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

Any of these occurrences could prevent us from achieving or maintaining market acceptance of the particular therapeutic candidate, if approved, and may harm our business, financial condition and prospects significantly.

Risks Related to Regulatory Review and Approval

Our clinical trials may fail to demonstrate substantial evidence of the safety and effectiveness of therapeutic candidates that we may identify and pursue for their intended uses, which would prevent, delay or limit the scope of regulatory clearance, authorization or approval and potential commercialization.

Before obtaining regulatory approvals for the commercial sale of any of our drug or biological therapeutic candidates, we must demonstrate through lengthy, complex and expensive preclinical studies and clinical trials that the applicable therapeutic candidate is both safe and effective for use in each target indication, and in the case of our Wholly Owned Programs and Founded Entities' therapeutic candidates regulated as biological therapeutics, that the therapeutic candidate is safe, pure and potent for use in its targeted indication. Each therapeutic candidate must demonstrate an adequate risk versus benefit profile in its intended patient population and for its intended use. Similarly, before obtaining regulatory clearances, authorization or approvals for the commercial sale of any of the device therapeutic candidates of our Founded Entities, our Founded Entities may be required to demonstrate through lengthy, complex and expensive preclinical studies and clinical trials that the applicable therapeutic candidate meets the regulatory standard of clearance, authorization or approval—for example, substantial equivalence or a reasonable assurance of safety or effectiveness, as applicable—for its intended use.

Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical development process. Most therapeutic candidates that

begin clinical trials are never approved by regulatory authorities for commercialization. We may be unable to design and execute a clinical trial to support marketing authorization.

We cannot be certain that our clinical trials will be successful. Additionally, any safety concerns observed in any one of our clinical trials in our targeted indications could limit the prospects for regulatory clearances, authorization or approval of our therapeutic candidates in those and other indications, which could have a material adverse effect on our business, financial condition and results of operations. In addition, even if such clinical trials are successfully completed, we cannot guarantee that the FDA, the EMA or comparable foreign regulatory authorities will interpret the results as we do, and more trials could be required before we submit our therapeutic candidates for clearance or approval. For example, the definition of clinical meaningfulness for outcome measures in lymphedema has not been firmly established by the FDA, introducing risk in evaluating and demonstrating the efficacy required to obtain FDA approval of LYT-100. As another example, while there is guidance regarding clinical meaningfulness for outcome measures in the context of acute COVID-19 treatments and potential vaccines, there is no such guidance for treatment of complications that persist following the resolution of COVID-19. Even if we believe that our and our Founded Entities' clinical trials and preclinical studies demonstrate the safety and efficacy of our and their therapeutic candidates, only the FDA and other comparable regulatory agencies may ultimately make such determination. No regulatory agency has made any such determination that any of our Wholly Owned Programs or those of our Founded Entities are safe or effective for use for any indication.

Additionally, we may utilize an "open-label" trial design for some of our future clinical trials. An open-label trial is one where both the patient and investigator know whether the patient is receiving the test article or either an existing approved drug or placebo. Open-label trials are subject to various limitations that may exaggerate any therapeutic effect as patients in open-label studies are aware that they are receiving treatment. Open-label trials may be subject to a "patient bias" where patients perceive their symptoms to have improved merely due to their awareness of receiving an experimental treatment. Patients selected for early clinical studies often include the most severe sufferers and their symptoms may have been bound to improve notwithstanding the new treatment. In addition, open-label trials may be subject to an "investigator bias" where those assessing and reviewing the physiological outcomes of the clinical trials are aware of which patients have received treatment and may interpret the information of the treated group more favorably given this knowledge. The opportunity for bias in clinical trials as a result of open-label design may not be adequately handled and may cause any of our trials that utilize such design to fail or to be considered inadequate and additional trials may be necessary to support future marketing applications. Moreover, results acceptable to support approval in one jurisdiction may be deemed inadequate by another regulatory authority to support regulatory approval in that other jurisdiction. To the extent that the results of the trials are not satisfactory to the FDA, the EMA or comparable foreign regulatory authorities for support of a marketing application, we may be required to expend significant resources, which may not be available to us, to conduct additional trials in support of potential approval of our Wholly Owned Programs. Even if regulatory approval is secured for a therapeutic candidate, the terms of such approval may limit the scope and use of the specific therapeutic candidate, which may also limit its commercial potential.

Even if we complete the necessary preclinical studies and clinical trials, the marketing approval process is expensive, time-consuming and uncertain and may prevent us from obtaining clearance, authorization or approvals for the potential commercialization of therapeutic candidates.

Any therapeutic candidate we may develop and the activities associated with their development and potential commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale and distribution, are subject to comprehensive regulation by the FDA, the EMA and other comparable foreign regulatory authorities. Failure to obtain marketing authorization for a therapeutic candidate will prevent us from commercializing the therapeutic candidate in a given jurisdiction. For example, although Gelesis and Akili have received marketing authorization for Plenity and EndeavorRx, respectively, from the FDA, we and our Founded Entities have not received clearance, authorization or approval to market any of our or their other therapeutic candidates from regulatory authorities in any jurisdiction and it is possible that none of the other therapeutic candidates we and our Founded Entities may seek to develop in the future will ever obtain regulatory clearance, authorization or approval. We have no experience in filing and supporting the applications necessary to gain marketing clearance, authorization or approval and expect to rely on third-party CROs or regulatory consultants to assist us in this process. Securing regulatory clearance, authorization or approval requires the submission of extensive preclinical and clinical data and supporting information to the various regulatory authorities for each therapeutic indication to establish the therapeutic candidate's safety, purity, efficacy and potency. Securing regulatory clearance, authorization or approval also requires the submission of information about the therapeutic manufacturing process to, and inspection of manufacturing facilities by, the relevant regulatory authority. Any therapeutic candidates we or our Founded Entities develop may not be effective, may be only moderately effective, or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining marketing clearance, authorization or approval or prevent or limit commercial use, if cleared, authorized or approved.

The process of obtaining marketing clearance, authorization or approval, both in the United States and abroad, is expensive, may take many years if additional clinical trials are required, if clearance, authorization or approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the therapeutic candidates involved. Changes in marketing authorization policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted therapeutic application, may cause delays in the clearance, authorization, approval or rejection of an application. The FDA and comparable authorities in other countries have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for clearance, authorization or approval and require additional preclinical, clinical or other studies. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit, or prevent marketing approval of a therapeutic candidate. Any marketing approval we ultimately obtain may be limited or subject to restrictions or post-market commitments that render the cleared, authorized or approved therapeutic not commercially viable.

If we experience delays in obtaining clearance, authorization or approval or if we fail to obtain clearance, authorization or approval of any therapeutic candidates we may develop, the commercial prospects for those therapeutic candidates may be harmed, and our ability to generate revenues will be materially impaired.

We have conducted, and may continue to conduct in the future, clinical trials for therapeutic candidates outside the United States, and the FDA, the EMA and comparable foreign regulatory authorities may not accept data from such trials.

We have conducted clinical trials outside of the United States in the past, and may in the future choose to conduct one or more clinical trials outside the United States, including in Europe. For example, we have conducted clinical trials in Australia and are conducting or may conduct clinical trials in additional locations outside the United States, including without limitation the U.K., Australia, Romania, Korea, Argentina, Poland and the Philippines. The acceptance of study data from clinical trials conducted outside the United States or another jurisdiction by the FDA, the EMA or any comparable foreign regulatory authority may be subject to certain conditions or may not be accepted at all. For example, in cases where data from foreign clinical trials are intended to serve as the basis for approval of a drug or biologic in the United States, the FDA will generally not approve the application on the basis of foreign data alone unless (i) the data are applicable to the U.S. population and U.S. medical practice; (ii) the trials were performed by clinical investigators of recognized competence and pursuant to GCP regulations; and (iii) if necessary, the FDA is able to validate the data through an on-site inspection or other appropriate means. In addition, even where the foreign study data are not intended to serve as the sole basis for approval, the FDA will not accept the data as support for an application for marketing approval unless the study is well-designed and well-conducted in accordance with GCP requirements and the FDA is able to validate the data from the study through an onsite inspection if deemed necessary. Many foreign regulatory authorities have similar approval requirements. In addition, such foreign trials would be subject to the applicable local laws of the foreign jurisdictions where the trials are conducted. There can be no assurance that the FDA, the EMA or any comparable foreign regulatory authority will accept data from trials conducted outside of the United States or the applicable jurisdiction. If the FDA, the EMA or any comparable foreign regulatory authority does not accept such data, it would result in the need for additional trials, which would be costly and time-consuming and delay aspects of our business plan, and which may result in therapeutic candidates that we may develop not receiving approval, authorization or clearance for commercialization in the applicable jurisdiction.

If we are unable to obtain regulatory clearance, authorization or approval in one or more jurisdictions for any therapeutic candidates that we may identify and develop, our business could be substantially harmed.

We cannot commercialize a therapeutic until the appropriate regulatory authorities have reviewed and cleared, authorized or approved the therapeutic candidate. Clearance, authorization or approval by the FDA, the EMA and comparable foreign regulatory authorities is lengthy and unpredictable, and depends upon numerous factors, including substantial discretion of the regulatory authorities. Clearance, authorization or approval

policies, regulations, or the type and amount of preclinical or clinical data necessary to gain clearance, authorization or approval may change during the course of a therapeutic candidate's development and may vary among jurisdictions, which may cause delays in the clearance, authorization or approval or the decision not to clear, authorize or approve an application. Gelesis and Akili have obtained marketing authorization from the FDA for Plenity and EndeavorRx, respectively, but we and our Founded Entities have not obtained regulatory clearance, authorization or approval for any other therapeutic candidates, and it is possible that our current therapeutic candidates and any other therapeutic candidates which we and our Founded Entities may seek to develop in the future will not ever obtain regulatory clearance, authorization or approval. We cannot be certain that any of our Wholly Owned Programs or our Founded Entities' therapeutic candidates will receive regulatory clearance, authorization or approval or be successfully commercialized even if we or our Founded Entities receive regulatory clearance, authorization or approval.

Obtaining marketing clearance, authorization or approval is an extensive, lengthy, expensive and inherently uncertain process, and regulatory authorities may delay, limit or deny clearance or clearance, authorization or approval of the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates for many reasons, including but not limited to:

- the inability to demonstrate to the satisfaction of the FDA, the EMA or comparable foreign regulatory authorities that the applicable therapeutic candidate is safe and effective as a treatment for our targeted indications or otherwise meets the applicable regulatory standards for clearance, authorization or approval;
- the FDA, the EMA or comparable foreign regulatory authorities may disagree with the design, endpoints or implementation of our or our Founded Entities' clinical trials;
- the population studied in the clinical program may not be sufficiently broad or representative to assure safety or efficacy in the full population for which we or our Founded Entities seek clearance, authorization or approval;
- the FDA, the EMA or comparable foreign regulatory authorities may require additional preclinical studies or clinical trials beyond those that we or our Founded Entities currently anticipate;
- the FDA, the EMA or comparable foreign regulatory authorities may disagree with our or our Founded Entities' interpretation of data from preclinical studies or clinical trials;
- the data collected from clinical trials of therapeutic candidates that we may identify and pursue may not be sufficient to support the submission of an NDA, biologics license application, or BLA, or other submission for regulatory clearance, authorization or approval in the United States or elsewhere;
- as applicable, we or our Founded Entities may be unable to demonstrate to the FDA, the EMA or comparable foreign regulatory authorities that a therapeutic candidate's risk-benefit ratio for its proposed indication is acceptable;
- the FDA, the EMA or comparable foreign regulatory authorities may identify deficiencies in the manufacturing processes, test procedures and specifications, or facilities of third-party manufacturers with which we or our Founded Entities contract for clinical and commercial supplies; and
- the clearance, authorization or approval policies or regulations of the FDA, the EMA or comparable foreign regulatory authorities may change in a manner that renders the clinical trial design or data insufficient for clearance or approval.

The lengthy approval process, as well as the unpredictability of the results of clinical trials and evolving regulatory requirements, may result in our or our Founded Entities' failure to obtain regulatory clearance, authorization or approval to market therapeutic candidates that we or our Founded Entities may pursue in the United States or elsewhere, which would significantly harm our or our Founded Entities' business, prospects, financial condition and results of operations.

Furthermore, clearance, authorization or approval by the FDA in the United States, if obtained, does not ensure approval by regulatory authorities in other countries or jurisdictions. In order to market any therapeutics outside of the United States, we or our Founded Entities must establish and comply with numerous and varying regulatory requirements of other countries regarding safety and effectiveness. Clinical trials conducted in one country may not be accepted by regulatory authorities in other countries, and regulatory approval in one country does not mean that regulatory approval will be obtained in any other country. Approval processes vary among countries and can involve additional therapeutic testing and validation and additional or different administrative review periods from those in the United States, including additional preclinical studies or clinical trials, as clinical trials conducted in one jurisdiction may not be accepted by regulatory authorities in other jurisdictions. In many jurisdictions outside the United States, a therapeutic candidate must be approved for reimbursement before it can be approved for sale in that jurisdiction. In some cases, the price that we intend to charge for our therapeutics is also subject to approval. Seeking foreign regulatory approval could result in difficulties and costs for us or our Founded Entities and require additional preclinical studies or clinical trials which could be costly and time-consuming. Regulatory requirements can vary widely from country to country and could delay or prevent the introduction of our or our Founded Entities' therapeutics in those countries. The foreign regulatory approval process involves all of the risks associated with FDA approval. We do not have any therapeutic candidates approved for sale in international markets, though two of our Founded Entities, Akili and Gelesis, do. If we or our Founded Entities fail to comply with regulatory requirements in international markets or to obtain and maintain required approvals, or if regulatory approvals in international markets are delayed, our target market will be reduced and our ability to realize the full market potential of our therapeutics will be harmed.

Interim, "top-line," and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available or as additional analyses are conducted, and as the data are subject to audit and verification procedures that could result in material changes in the final data.

From time to time, we may publish interim, "top-line," or preliminary data from our clinical studies. Data from interim analyses of clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Preliminary or "top-line" data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, interim, "top-line.," and preliminary data should be viewed with caution until the final data are available. Material adverse changes between preliminary, "top-line," or interim data and final data could significantly harm our business prospects.

Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular therapeutic candidate or therapeutic and our company in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is the material or otherwise appropriate information to include in our disclosure. Any information we determine not to disclose may ultimately be deemed significant by you or others with respect to future decisions, conclusions, views, activities or otherwise regarding a particular therapeutic candidate or our business.

The complexity of a combination therapeutic that includes a drug or biologic and a medical device presents additional, unique development and regulatory challenges, which may adversely impact our or our Founded Entities' development plans and our or our Founded Entities' ability to obtain regulatory clearance, authorization or approval of our Wholly Owned Programs or our Founded Entities' therapeutic candidates.

We or our Founded Entities, such as Follica, may decide to pursue marketing authorization of a combination therapeutic. A combination therapeutic may include, amongst other possibilities, any investigational drug, device, or biologic packaged separately that according to its proposed labeling is for use only with another individually specified investigational drug, device, or biologic where both are required to achieve the intended use, indication, or effect.

Developing and obtaining regulatory clearance, authorization or approval for combination therapeutics pose unique challenges because they involve components that are regulated by the FDA under different types of regulatory requirements, and by different FDA centers. As a result, such therapeutics raise regulatory, policy and review management challenges. For example, because divisions from both FDA's Center for Drug Evaluation and Research or Center for Biologics Evaluation and Research and FDA's Center for Devices and Radiological Health must review submissions concerning therapeutic candidates that are combination therapeutics comprised of drug or biologics and devices, respectively, the regulatory review and clearance, authorization or approval process for these therapeutics may be lengthened. In addition, differences in regulatory pathways for each component of a combination therapeutic can impact the regulatory processes for all aspects of therapeutic development and management, including clinical investigation, marketing applications, manufacturing and quality control, adverse event reporting, promotion and advertising, user fees and post-clearance, authorization or approval modifications. Similarly, if applicable, the device components of a combination therapeutic candidate will require any necessary clearances or approvals or other marketing authorizations in other jurisdictions, which may prove challenging to obtain.

Certain modifications to our Founded Entities' device therapeutics may require new 510(k) clearance or other marketing authorizations and may require our Founded Entities to recall or cease marketing their therapeutics.

Akili and Gelesis received de novo classification for EndeavorRx and Plenity, respectively, from the FDA. Once a medical device is permitted to be legally marketed in the United States pursuant to a 510(k) clearance, de novo classification, or a premarket approval, or PMA, a manufacturer may be required to notify the FDA of certain modifications to the device. Manufacturers determine in the first instance whether a change to a medical device requires a new premarket submission, but the FDA may review any manufacturer's decision. The FDA may not agree with our Founded Entities' decisions regarding whether new clearances, authorizations or approvals are necessary. They may make modifications or add additional features in the future that they believe do not require a new 510(k) clearance, de novo marketing authorization, or approval of a PMA or PMA amendments or supplements. If the FDA disagrees with their determinations and requires them to submit new 510(k) notifications, requests for de novo classification, or PMAs (or PMA supplements or amendments) for modifications to their previously cleared or authorized therapeutics for which they have concluded that new clearances, authorization or approvals are unnecessary, they may be required to cease marketing or to recall the modified therapeutic until they obtain clearance, authorization or approval, and they may be subject to significant regulatory fines or penalties.

The regulatory landscape that will apply to development of therapeutic candidates by us or our Founded Entities or collaborators is rigorous, complex, uncertain and subject to change, which could result in delays or termination of development of such therapeutic candidates or unexpected costs in obtaining regulatory approvals.

We or our Founded Entities or collaborators may develop therapeutic candidates that use genome or cell editing technologies. Regulatory requirements governing therapeutics created with genome editing technology or involving gene therapy treatment have changed frequently and will likely continue to change in the future. Approvals by one regulatory agency may not be indicative of what any other regulatory agency may require for approval, and there is substantial, and sometimes uncoordinated, overlap in those responsible for regulation of gene therapy therapeutics, cell therapy therapeutics and other therapeutics created with genome editing technology. For example, the FDA established the Office of Tissues and Advanced Therapies within its Center for Biologics Evaluation and Research, or CBER, to consolidate the review of gene therapy and related therapeutics, and the Cellular, Tissue and Gene Therapies Advisory Committee to advise CBER on its review. These and other regulatory review agencies, committees and advisory groups and the requirements and guidelines they promulgate may lengthen the regulatory review process, require us or our Founded Entities to perform additional preclinical studies or clinical trials, increase our or our Founded Entities' development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of these treatment candidates or lead to significant post-approval limitations or restrictions.

Additionally, under the National Institutes of Health, or NIH, Guidelines for Research Involving Recombinant Synthetic Nucleic Acid Molecules, or NIH Guidelines, supervision of human gene transfer trials includes evaluation and assessment by an institutional biosafety committee, or IBC, a local institutional committee that reviews and oversees research utilizing recombinant or synthetic nucleic acid molecules at that institution. The IBC assesses the safety of the research and identifies any potential risk to public health or the environment, and such review may result in some delay before initiation of a clinical trial. While the NIH Guidelines are not mandatory unless the research in question is being conducted at or sponsored by institutions receiving NIH funding of recombinant or synthetic nucleic acid molecule research, many companies and other institutions not otherwise subject to the NIH Guidelines voluntarily follow them.

In the EEA, the EMA has a Committee for Advanced Therapies, or CAT, that is responsible for assessing the quality, safety and efficacy of advanced therapy medicinal therapeutics. Advanced-therapy medicinal therapeutics include gene therapy medicines, somatic-cell therapy medicines and tissue-engineered medicines. The role of the CAT is to prepare a draft opinion on an application for marketing authorization for an advanced therapy medicinal candidate that is submitted to the EMA. In the EEA, the development and evaluation of a gene therapy medicinal therapeutic must be considered in the context of the relevant EMA guidelines. The EMA may issue new guidelines concerning the development and marketing authorization for gene therapy medicinal therapeutics and require that we or our Founded Entities comply with these new guidelines. Similarly complex regulatory environments exist in other jurisdictions in which we or our Founded Entities might consider seeking regulatory approvals for our Wholly Owned Programs or our Founded Entities' therapeutic candidates, further complicating the regulatory landscape. As a result, the procedures and standards applied to gene therapy therapeutics and cell therapy therapeutics may be applied to any of our or our Founded Entities' gene therapy or genome editing therapeutic candidates, but that remains uncertain at this point.

Changes in applicable regulatory guidelines may lengthen the regulatory review process for the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates, require additional studies or trials, increase development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of such therapeutic candidates, or lead to significant post-approval limitations or restrictions. Additionally, adverse developments in clinical trials conducted by others of gene therapy therapeutics or therapeutics created using genome editing technology, or adverse public perception of the field of genome editing, may cause the FDA, the EMA and other regulatory bodies to revise the requirements for approval of any therapeutic candidates we or our Founded Entities may develop or limit the use of therapeutics utilizing genome editing technologies, either of which could materially harm our or our Founded Entities' business. Furthermore, regulatory action or private litigation could result in expenses, delays or other impediments to our research programs or the development or commercialization of current or future therapeutic candidates.

As we advance therapeutic candidates alone or with collaborators, we will be required to consult with these regulatory and advisory groups and comply with all applicable guidelines, rules and regulations. If we fail to do so, we or our collaborators may be required to delay or terminate development of such therapeutic candidates. Delay or failure to obtain, or unexpected costs in obtaining, the regulatory approval necessary to bring a therapeutic candidate to market could decrease our ability to generate sufficient therapeutic revenue to maintain our business.

We may not elect or be able to take advantage of any expedited development or regulatory review and approval processes available to drug therapeutic candidates granted breakthrough therapy or fast track designation by the FDA.

We intend to evaluate and continue ongoing discussions with the FDA on regulatory strategies that could enable us or our Founded Entities to take advantage of expedited development pathways for certain of our Wholly Owned Programs or our Founded Entities' therapeutic candidates in the future, although we cannot be certain that our Wholly Owned Programs or our Founded Entities' therapeutic candidates will qualify for any expedited development pathways or that regulatory authorities will grant, or allow us or our Founded Entities to maintain, the relevant qualifying designations. Potential expedited development pathways that we could pursue include breakthrough therapy and fast track designation.

Breakthrough therapy designation is intended to expedite the development and review of drug and biologic therapeutic candidates that are designed to treat serious or life-threatening diseases when preliminary clinical evidence indicates that the drug or biologic may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The designation of a therapeutic candidate as a breakthrough therapy provides potential benefits that include more frequent meetings with FDA to discuss the development plan for the therapeutic candidate and ensure collection of appropriate data needed to support approval; more frequent written correspondence from FDA about such things as the design of the proposed clinical trials and use of biomarkers; intensive guidance on an efficient drug development program, beginning as early as Phase 1; organizational commitment involving senior managers; and eligibility for rolling review and priority review of an NDA or BLA. Fast track designation is designed for therapeutic candidates intended for the treatment of a serious or life-threatening disease or condition, where preclinical or clinical data demonstrate the potential to address an unmet medical need for this disease or condition. The sponsor of a fast track therapeutic candidate has opportunities for more frequent interactions with the FDA review team during product development and, once an NDA or BLA is submitted, the application may be eligible for rolling review.

Even if we believe a particular therapeutic candidate is eligible for breakthrough therapy or fast track designation, we cannot assure you that the FDA would decide to grant it. Breakthrough therapy designation and fast track designation do not change the standards for approval, and there is no assurance that such designation or eligibility will result in expedited review or approval. Thus, even if we or our Founded Entities do receive breakthrough therapy or fast track designation, we or our Founded Entities may not experience a faster development process, review or approval compared to conventional FDA procedures. The FDA may withdraw breakthrough therapy or fast track designation if it believes that the therapeutic no longer meets the qualifying criteria. Our business may be harmed if we are unable to avail ourselves of these or any other expedited development and regulatory pathways.

We may not be able to obtain or maintain orphan drug designation or exclusivity for our therapeutic candidates.

Regulatory authorities in some jurisdictions, including the United States, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a drug as an orphan drug if it is intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals in the United States, or if the disease or condition affects more than 200,000 individuals in the United States and there is no reasonable expectation that the cost of developing the drug for the type of disease or condition will be recovered from sales of the product in the United States.

Orphan drug designation entitles a party to financial incentives, such as tax advantages and user fee waivers. Additionally, if a product that has orphan designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to orphan drug exclusivity, which means that the FDA may not approve any other applications to market the same drug for the same disease or condition for seven years, except in certain circumstances, such as a showing of clinical superiority (i.e., another product is safer, more effective or makes a major contribution to patient care) over the product with orphan exclusivity or where the manufacturer is unable to assure sufficient product quantity. Competitors, however, may receive approval of different products for the same disease or condition for which the orphan product has exclusivity, or obtain approval for the same product but for a different disease or condition than that for which the orphan product has exclusivity.

We have obtained orphan drug designation in the United States for LYT-200 for the treatment of pancreatic cancer, and we may also seek orphan drug designation for other of our therapeutic candidates in the future. We may not be the first to obtain regulatory approval of any therapeutic candidate for its orphan-designated disease or condition and may therefore not obtain orphan drug exclusivity. In addition, exclusive marketing rights in the United States may be limited if we seek approval for an disease or condition broader than the orphan-designated disease or condition or may be lost if the FDA later determines that the request for orphan designation was materially defective or if the manufacturer is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition. Orphan drug designation does not ensure that we will receive marketing exclusivity in a particular market, and we cannot assure you that any future application for orphan drug designation with respect to any other therapeutic candidate will be granted. Orphan drug designation neither shortens the development time or regulatory review time of a drug, nor gives the drug any advantage in the regulatory review or approval process.

If we or our Founded Entities are unable to successfully validate, develop and obtain regulatory clearance, authorization or approval for companion diagnostic tests for any future drug candidates that require or would commercially benefit from such tests, or experience significant delays in doing so, we or our Founded Entities may not realize the full commercial potential of these drug candidates.

In connection with the clinical development of the therapeutic candidates within our Wholly Owned Pipeline or Founded Entities' therapeutic candidates for certain indications, we or our Founded Entities may work with collaborators to develop or obtain access to in vitro companion diagnostic tests to identify patient subsets within a disease category who may derive selective and meaningful benefit from our drug candidates. For example, we may elect to develop companion diagnostics for LYT-200 and LYT-210. To be successful, we, our Founded Entities or our collaborators will need to address a number of scientific, technical, regulatory and logistical challenges. The FDA, the EMA and comparable foreign regulatory authorities regulate in vitro companion diagnostics as medical devices and, under that regulatory framework, will likely require the conduct of clinical trials to demonstrate the safety and effectiveness of any diagnostics we or our Founded Entities may develop, which we expect will require separate regulatory clearance, authorization or approval prior to commercialization. In addition, if safe and effective use of a therapeutic product depends on an in vitro companion diagnostic, the FDA generally will require approval, authorization or clearance of that diagnostic, known as a companion diagnostic, before or at the same time that the FDA approves the therapeutic product.

We or our Founded Entities may rely on third parties for the design, development and manufacture of companion diagnostic tests for our Wholly Owned Programs or our Founded Entities' therapeutic candidates that may require such tests. If we or our Founded Entities enter into such collaborative agreements, we will be dependent on the sustained cooperation and effort of our future collaborators in developing and obtaining approval for these companion diagnostics. It may be necessary to resolve issues such as selectivity/specificity, analytical validation, reproducibility, or clinical validation of companion diagnostics during the development and regulatory clearance, authorization or approval processes. Moreover, even if data from preclinical studies and early clinical trials appear to support development of a companion diagnostic for a therapeutic candidate, data generated in later clinical trials may fail to support the analytical and clinical validation of the companion diagnostic. We, our Founded Entities and our future collaborators may encounter difficulties in developing, obtaining regulatory clearance, authorization or approval for, manufacturing and commercializing companion diagnostics similar to those we face with respect to the therapeutic candidates within our Wholly Owned Pipeline themselves, including issues with achieving regulatory clearance, authorization or approval, production of sufficient quantities at commercial scale and with appropriate quality standards, and in gaining market acceptance. If we or our Founded Entities are unable to successfully develop companion diagnostics for these therapeutic candidates, or experience delays in doing so, the development of these therapeutic candidates may be adversely affected, these therapeutic candidates may not obtain marketing approval, and we may not realize the full commercial potential of any of these therapeutic candidates that obtain marketing approval. As a result, our business, results of operations and financial condition could be materially harmed. In addition, a diagnostic company with whom we or our Founded Entities contract may decide to discontinue selling or manufacturing the companion diagnostic test that we anticipate using in connection with development and commercialization of our Wholly Owned Programs or our Founded Entities' therapeutic candidates or our relationship with such diagnostic company may otherwise terminate. We or our Founded Entities may not be able to enter into arrangements with another diagnostic company to obtain supplies of an alternative diagnostic test for use in connection with the development and commercialization of our Wholly Owned Programs or our Founded Entities' therapeutic candidates or do so on commercially reasonable terms, which could adversely affect and/or delay the development or commercialization of our or our Founded Entities' therapeutic candidates.

For any cleared, authorized or approved therapeutic, we or our Founded Entities will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense and we or our Founded Entities may be subject to penalties if we or our Founded Entities fail to comply with regulatory requirements or experience unanticipated problems with the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates.

Gelesis' Plenity and Akili's EndeavorRx are, and any of the therapeutic candidates within our Wholly Owned Programs or our Founded Entities' therapeutic candidates that are cleared, authorized or approved will be, subject to ongoing regulatory requirements for manufacturing, labeling, packaging, storage, advertising, promotion, sampling, record-keeping, conduct of post-marketing studies, and submission of safety, efficacy and other post-market information, including both federal and state requirements in the United States and requirements of comparable foreign regulatory authorities.

Manufacturers and manufacturers' facilities are required to comply with extensive requirements imposed by the FDA, the EMA and other comparable foreign regulatory authorities, including ensuring that quality control and manufacturing procedures conform to current good manufacturing practices, or cGMP, regulations. As such, we and our CMOs are subject to continual review and inspections to assess compliance with cGMP and adherence to commitments made in any marketing authorization, and any future 510(k), de novo classification, PMA, NDA, BLA or marketing authorization application, or MAA, or equivalent application. We and our CMOs are also subject to requirements pertaining to the registration of our manufacturing facilities and the listing of our and our Founded Entities' therapeutics and therapeutic candidates with the FDA; continued complaint, adverse event and malfunction reporting; corrections and removals reporting; and labeling and promotional requirements. Accordingly, we and others with whom we work must continue to expend time, money, and effort in all areas of regulatory compliance, including manufacturing, production and quality control. Gelesis' and Akili's marketing authorizations for Plenity and EndeavorRx, respectively, are and any regulatory clearances, authorization or approvals that we may receive for the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates will be, subject to limitations on the cleared, authorized or approved indicated uses for which the therapeutic may be marketed and promoted or to the conditions of approval. Any regulatory clearances, authorizations or approvals that we may receive for the therapeutic candidates within our Wholly Owned Pipeline may contain requirements for potentially costly post-marketing testing, such as Phase 4 clinical trials and surveillance to monitor the safety and efficacy of a drug therapeutic. We are required to report certain adverse reactions and production problems, if any, to the FDA, the EMA and other comparable foreign regulatory authorities. Any new legislation addressing drug or medical safety issues could result in delays in therapeutic development or commercialization, or increased costs to assure compliance.

The FDA and other agencies, including the U.S. Department of Justice, and for certain therapeutics, the Federal Trade Commission, closely regulate and monitor the marketing, labeling, advertising and promotion of therapeutics to ensure that they are manufactured, marketed and

distributed only for the cleared, authorized or approved indications and in accordance with the provisions of the cleared, authorized or approved labeling. We are, and will be, required to comply with requirements concerning advertising and promotion for the therapeutic candidates within our Wholly Owned Pipeline, if cleared, authorized or approved. For example, promotional communications with respect to prescription drugs and medical devices are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the therapeutic's label or labeling. We may not promote our therapeutics for indications or uses for which they do not have approval, authorization or clearance.

The holder of a cleared 510(k), de novo classification, or an approved NDA, BLA, PMA, MAA or equivalent marketing authorization must submit new or supplemental applications and obtain clearance, authorization or approval for certain changes to the approved therapeutic, therapeutic labeling, or manufacturing process. For example, any modification to Plenity or EndeavorRx that could significantly affect its safety or effectiveness or that would constitute a major change in its intended use could require a new 510(k) clearance, de novo classification or approval of PMA application. Delays in obtaining required clearances or approvals would harm our ability to introduce new or enhanced therapeutic in a timely manner, which in turn would harm our or our Founded Entities' future growth. Failure to submit a new or supplemental application and to obtain approval for certain changes prior to marketing the modified therapeutic may require a recall or to stop selling or distributing the marketed therapeutic as modified, and may lead to significant enforcement actions.

In the European Economic Area, or the EEA, any medical devices will need to comply with the Essential Requirements set forth in the new Medical Device Regulation (EU) 2017/745, which became fully applicable on May 26, 2021. Compliance with these requirements is a prerequisite to be able to affix the CE mark to a therapeutic, without which a therapeutic cannot be marketed or sold in the EEA. To demonstrate compliance with the Essential Requirements and obtain the right to affix the CE mark, we or our Founded Entities must undergo a conformity assessment procedure, which varies according to the type of medical device and its classification. The conformity assessment procedure requires the intervention of a Notified Body (except for certain class I devices), which is an organization designated by a competent authority of an EEA country to conduct conformity assessments. The Notified Body issues a CE Certificate of Conformity following successful completion of a conformity assessment procedure and quality management system audit conducted in relation to the medical device and its manufacturer and their conformity with the Essential Requirements. This Certificate entitles the manufacturer to affix the CE mark to its medical therapeutics after having prepared and signed a related EC Declaration of Conformity. In June 2020, Gelesis received a CE Mark for Plenity as a class III medical device indicated for weight loss in overweight and obese adults with a Body Mass Index of 25-40 kg/m2, when used in conjunction with diet and exercise. Also in June 2020, Akili received a CE Mark for EndeavorRx as a prescription-only digital therapeutic software intended for the treatment of attention and inhibitory control deficits in paediatric patients with ADHD.

We or our Founded Entities could also be required to conduct post-marketing clinical trials to verify the safety and efficacy of our or our Founded Entities' therapeutics in general or in specific patient subsets. If original marketing approval of a drug or biologic was obtained via an accelerated approval pathway, we or our Founded Entities could be required to conduct a successful post-marketing clinical trial to confirm clinical benefit for our or our Founded Entities' therapeutics. An unsuccessful post-marketing study or failure to complete such a study could result in the withdrawal of marketing clearance, authorization or approval.

If a regulatory agency discovers previously unknown problems with a therapeutic, such as AEs of unanticipated severity or frequency, or problems with the facility where the therapeutic is manufactured, or disagrees with the promotion, marketing or labeling of a therapeutic, such regulatory agency may impose restrictions on that therapeutic or us, including requiring withdrawal of the therapeutic from the market. If we or our Founded Entities fail to comply with applicable regulatory requirements, a regulatory agency or enforcement authority may, among other things:

- issue warning letters that would result in adverse publicity;
- impose civil or criminal penalties;
- suspend or withdraw regulatory approvals;
- suspend any of our or our Founded Entities' ongoing clinical trials;
- refuse to approve pending applications or supplements to approved applications submitted by us or our Founded Entities;
- impose restrictions on our operations, including closing our CMOs' facilities;
- seize or detain therapeutics; or
- require a recall.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response, and could generate negative publicity. Any failure to comply with ongoing regulatory requirements may significantly and adversely affect our ability to commercialize and generate revenue from our therapeutics. If regulatory sanctions are applied or if regulatory clearance, authorization or approval is withdrawn, the value of our company and our operating results will be adversely affected.

The FDA's and other regulatory authorities' policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory clearance, authorization or approval of the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates.

We also cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If these legislative or administrative actions impose constraints on the FDA's ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted.

The FDA and other regulatory agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses.

If, for any of our Wholly Owned Programs that are cleared or approved, we are found to have improperly promoted off-label uses of those therapeutics, we may become subject to significant liability. The FDA and other regulatory agencies strictly regulate the promotional claims that may be made about prescription therapeutics, if cleared, authorized or approved. In particular, while the FDA permits the dissemination of truthful and non-misleading information about a cleared, authorized or approved therapeutic, a manufacturer may not promote a therapeutic for uses that are not cleared, authorized or approved by the FDA or such other regulatory agencies as reflected in the therapeutic's cleared, authorized or approved labeling. If we are found to have promoted such off-label uses, we may become subject to significant liability. The federal government has levied large civil and criminal fines against companies for alleged improper promotion of off-label use and has enjoined several companies from engaging in off-label promotion. The FDA has also requested that companies enter into consent decrees, corporate integrity agreements or permanent injunctions under which specified promotional conduct must be changed or curtailed. If we cannot successfully manage the promotion of the therapeutic candidates within our Wholly Owned Pipeline, if cleared, authorized or approved, we could become subject to significant liability, which would materially adversely affect our business and financial condition.

Risks Related to Manufacturing our Therapeutic Candidates or Those of our Founded Entities

Certain of the therapeutic candidates being developed by us or our Founded Entities are novel, complex and difficult to manufacture. We could experience manufacturing problems that result in delays in our development or commercialization programs or otherwise harm our business.

The manufacturing processes our CMOs use to produce our and our Founded Entities' therapeutic candidates are complex and in certain cases novel. Several factors could cause production interruptions, including inability to develop novel manufacturing processes, equipment malfunctions, facility contamination, raw material shortages or contamination, natural disasters, disruption in utility services, human error or disruptions in the operations of our suppliers, including acquisition of the supplier by a third party or declaration of bankruptcy. For example, Vedanta has its own proprietary cGMP manufacturing facilities for certain therapeutic candidates, including VE202, VE303, VE800 and VE416. Creating defined consortia of live microbial therapeutics for these therapeutic candidates is inherently complex, and therefore can be vulnerable to delays. The expertise required to manufacture these therapeutic candidates is unique to Vedanta, and as a result, it would be difficult and time consuming to find an alternative CMO. In addition, manufacturing of clinical supply for certain of our therapeutic candidates is dependent on third party CMOs, and manufacturing such therapeutic candidates is inherently complex. As another example, we are advancing LYT-100 for potential treatment of complications that persist following the resolution of COVID-19 infection. COVID-19 has been widespread, and any approved treatments related to COVID-19 could face issues manufacturing sufficient quantities to meet demand. Additionally, two vaccines for COVID-19 have received full approval by the FDA and one other vaccine for COVID-19 was granted Emergency Use Authorization by the FDA. The resultant demand for vaccines and potential for manufacturing facilities and materials to be commandeered under the Defense Production Act of 1950, or equivalent foreign legislation, may make it more difficult to obtain materials or manufacturing slots for the therapeutics needed for our and our Founded Entities' clinical trials or therapeutics which could lead to delays in these trials or supply shortages of therapeutics.

Some of our and our Founded Entities' therapeutic candidates include biologics, some of which have physical and chemical properties that cannot be fully characterized. As a result, assays of the finished product may not be sufficient to ensure that the therapeutic candidate is consistent from lot-to-lot or will perform in the intended manner. Accordingly, our CMOs must employ multiple steps to control the manufacturing process to assure that the process is reproducible and the therapeutic candidate is made strictly and consistently in compliance with the process. Problems with the manufacturing process, even minor deviations from the normal process, could result in therapeutic defects or manufacturing failures that result in lot failures, therapeutic recalls, product liability claims or insufficient inventory to conduct clinical trials or supply commercial markets. We or our Founded Entities may encounter problems achieving adequate quantities and quality of clinical-grade materials that meet the FDA, the EMA or other applicable standards or specifications with consistent and acceptable production yields and costs.

In addition, the FDA, the EMA and other foreign regulatory authorities may require us or our Founded Entities to submit samples of any lot of any approved therapeutic together with the protocols showing the results of applicable tests at any time. Under some circumstances, the FDA, the EMA or other foreign regulatory authorities may require that we or our Founded Entities not distribute a lot until the agency authorizes its release. Slight deviations in the manufacturing process, including those affecting quality attributes and stability, may result in unacceptable changes in the therapeutic that could result in lot failures or therapeutic recalls. Lot failures or therapeutic recalls could cause us or our Founded Entities to delay therapeutic launches or clinical trials, which could be costly to us and otherwise harm our business, financial condition, results of operations and prospects.

Our CMOs also may encounter problems hiring and retaining the experienced scientific, quality assurance, quality-control and manufacturing personnel needed to operate our manufacturing processes, which could result in delays in production or difficulties in maintaining compliance with applicable regulatory requirements.

Any problems in our CMOs' manufacturing process or facilities could result in delays in planned clinical trials and increased costs, and could make us a less attractive collaborator for potential partners, including larger biotechnology companies and academic research institutions, which could limit access to additional attractive development programs. Problems in our manufacturing process could restrict our ability to meet potential future market demand for therapeutics.

We do not currently have nor do we plan to acquire the infrastructure or capability internally to manufacture our clinical drug supplies for use in the conduct of our clinical trials, and we lack the resources and the capability to manufacture the therapeutic candidates within our Wholly Owned Pipeline on a clinical or commercial scale. Instead, we rely on our third-party manufacturing partners for the production of the active pharmaceutical ingredient, or API, and drug formulation. The facilities used by our third-party manufacturers to manufacture our therapeutic candidates that we may develop must be successfully inspected by the applicable regulatory authorities, including the FDA, after we submit any NDA or BLA to the FDA.

We are currently completely dependent on our third-party manufacturers for the production of certain of our therapeutic candidates in accordance with cGMPs, which include, among other things, quality control, quality assurance and the maintenance of records and documentation.

Although we have entered into agreements for the manufacture of clinical supplies for such therapeutic candidates, our third-party manufacturers may not perform as agreed, may be unable to comply with these cGMP requirements and with FDA, state and foreign regulatory requirements or may terminate its agreement with us. If any of our third-party manufacturers cannot successfully manufacture material that conforms to our specifications and the applicable regulatory authorities' strict regulatory requirements, pass regulatory inspection or maintain a compliance status acceptable to the FDA or state or foreign regulatory authorities, our NDAs or BLAs will not be approved. In addition, although we are ultimately responsible for ensuring therapeutic quality, we have no direct day-to-day control over our third-party manufacturers' ability to maintain adequate quality control, quality assurance and qualified personnel. If our third-party manufacturers are unable to satisfy the regulatory requirements for the manufacture of our therapeutics, if approved, or if our suppliers or third-party manufacturers decide they no longer want to manufacture our therapeutics, we will need to find alternative manufacturing facilities, which would be time-consuming and significantly impact our ability to develop, obtain regulatory approval for or market our therapeutics, if approved. If we are required to change contract manufacturers for any reason, we will be required to show that the new manufacturer maintains facilities and procedures that comply with quality standards and with all applicable regulations. We will also need to verify, such as through a manufacturing comparability study, that any new manufacturing process or procedure will produce our therapeutic candidate according to specifications previously submitted to the FDA or another regulatory authority. We might be unable to identify manufacturers for long-term clinical and commercial supply on acceptable terms or at all. Manufacturers are subject to ongoing periodic announced and unannounced inspection by the FDA and other governmental authorities to ensure compliance with government regulations. As a result, our third-party manufacturers may be subject to increased scrutiny.

If we were to experience an unexpected loss of supply for clinical development or commercialization, we could experience delays in our ongoing or planned clinical trials as our third-party manufacturers would need to manufacture additional quantities of our clinical and commercial supply and we may not be able to provide sufficient lead time to enable our third-party manufacturers to schedule a manufacturing slot, or to produce the necessary replacement quantities. This could result in delays in progressing our clinical development activities and achieving regulatory approval for our therapeutics, which could materially harm our business.

The manufacture of pharmaceutical therapeutics is complex and requires significant expertise and capital investment, including the development of advanced manufacturing techniques and process controls. We and our contract manufacturers must comply with cGMP regulations and guidelines. Manufacturers of pharmaceutical therapeutics often encounter difficulties in production, particularly in scaling up and validating initial production. These problems include difficulties with production costs and yields, quality control, including stability of the product, quality assurance testing, operator error, shortages of qualified personnel, as well as compliance with strictly enforced federal, state and foreign regulations. Furthermore, if microbial, viral or other contaminations are discovered in our therapeutics or in the manufacturing facilities in which our therapeutics, if approved, are made, such manufacturing facilities may need to be closed for an extended period of time to investigate and remedy the contamination. We cannot assure you that any stability or other issues relating to the manufacture of any of our therapeutics will not occur in the future. Additionally, our manufacturers may experience manufacturing difficulties due to resource constraints or as a result of labor disputes or unstable political environments. If our manufacturers were to encounter any of these difficulties, or otherwise fail to comply with their contractual obligations, our ability to provide any therapeutic candidates to patients in clinical trials would be jeopardized. Any delay or interruption in the supply of clinical trial supplies could delay the completion of clinical trials, increase the costs associated with maintaining clinical trial programs and, depending upon the period of delay, require us to commence new clinical trials at additional expense or terminate clinical trials completely.

Any adverse developments affecting clinical or commercial manufacturing of our therapeutics may result in shipment delays, inventory shortages, lot failures, therapeutic withdrawals or recalls, or other interruptions in the supply of our therapeutics or therapeutic candidates. We may also have to take inventory write-offs and incur other charges and expenses for therapeutics or therapeutic candidates that fail to meet specifications, undertake costly remediation efforts or seek more costly manufacturing alternatives. Accordingly, failures or difficulties faced at any level of our supply chain could materially adversely affect our business and delay or impede the development and commercialization of any of our therapeutics or therapeutic candidates and could have a material adverse effect on our business, prospects, financial condition and results of operations.

Our or our Founded Entities' therapeutics must be manufactured in accordance with federal, state and international regulations, and we or our Founded Entities could be forced to recall our or our Founded Entities' medical devices or terminate production if we or our Founded Entities fail to comply with these regulations.

The methods used in, and the facilities used for, the manufacture of medical device therapeutics of our Founded Entities, including Gelesis, Akili, Follica and Sonde, must comply with the FDA's cGMPs for medical devices, known as Quality System Regulation, or QSR, which is a complex regulatory scheme that covers the procedures and documentation of, among other requirements, the design, testing, validation, verification, complaint handling, production, process controls, quality assurance, labeling, supplier evaluation, packaging, handling, storage, distribution, installation, servicing and shipping of medical devices. Furthermore, we and our Founded Entities are required to verify that our suppliers maintain facilities, procedures and operations that comply with our quality standards and applicable regulatory requirements. The FDA enforces the QSR through, among other oversight methods, periodic announced or unannounced inspections of medical device manufacturing facilities, which may include the facilities of subcontractors, suppliers or CMOs. Our and our Founded Entities' therapeutics are also subject to similar state regulations and various laws and regulations of foreign countries governing manufacturing.

Our or our Founded Entities' third-party manufacturers may not take the necessary steps to comply with applicable regulations or our or our Founded Entities' specifications, which could cause delays in the delivery of our therapeutics. In addition, failure to comply with applicable FDA requirements or later discovery of previously unknown problems with our or our Founded Entities' therapeutics or manufacturing processes could result in, among other things: warning letters or untitled letters; civil penalties; suspension or withdrawal of approvals or clearances; seizures or recalls of

our or our Founded Entities' therapeutics; total or partial suspension of production or distribution; administrative or judicially imposed sanctions; the FDA's refusal to grant pending or future clearances or approvals for our or our Founded Entities' therapeutics; clinical holds; refusal to permit the import or export of our or our Founded Entities' therapeutics; and criminal prosecution of us or our employees. Any of these actions could significantly and negatively impact supply of our or our Founded Entities' therapeutics. If any of these events occurs, our reputation could be harmed, we could be exposed to product liability claims and we or our Founded Entities could lose customers and suffer reduced revenue and increased costs.

Risks Related to Commercialization

If, in the future, we are unable to establish sales and marketing capabilities or enter into agreements with third parties to sell and market any therapeutic candidates we may develop, we may not be successful in commercializing those therapeutic candidates if and when they are approved.

We do not have a sales or marketing infrastructure or the capabilities for sale, marketing, or distribution of pharmaceutical therapeutics. To achieve commercial success for any approved therapeutic for which we retain sales and marketing responsibilities, we must either develop a sales and marketing organization or outsource these functions to third parties. In the future, we may choose to build a focused sales, marketing, and commercial support infrastructure to market and sell the therapeutic candidates within our Wholly Owned Pipeline, if and when they are approved. We may also elect to enter into collaborations or strategic partnerships with third parties to engage in commercialization activities with respect to selected therapeutic candidates, indications or geographic territories, including territories outside the United States, although there is no guarantee we will be able to enter into these arrangements even if the intent is to do so.

There are risks involved with both establishing our own commercial capabilities and entering into arrangements with third parties to perform these services. For example, recruiting and training a sales force or reimbursement specialists is expensive and time consuming and could delay any therapeutic launch. If the commercial launch of a therapeutic candidate for which we recruit a sales force and establish marketing and other commercialization capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition commercialization personnel.

Factors that may inhibit our efforts to commercialize any approved therapeutic on our own include:

- the inability to recruit and retain adequate numbers of effective sales, marketing, reimbursement, customer service, medical affairs, and other support personnel;
- the inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe any future approved therapeutics;
- the inability of reimbursement professionals to negotiate arrangements for formulary access, reimbursement, and other acceptance by payors;
- the inability to price therapeutics at a sufficient price point to ensure an adequate and attractive level of profitability;
- restricted or closed distribution channels that make it difficult to distribute our therapeutics to segments of the patient population;
- the lack of complementary therapeutics to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive therapeutic lines; and
- unforeseen costs and expenses associated with creating an independent commercialization organization.

If we enter into arrangements with third parties to perform sales, marketing, commercial support, and distribution services, our therapeutic revenue or the profitability of therapeutic revenue may be lower than if we were to market and sell any therapeutics we may develop internally. In addition, we may not be successful in entering into arrangements with third parties to commercialize the therapeutic candidates within our Wholly Owned Pipeline or may be unable to do so on terms that are favorable to us or them. We may have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our therapeutics effectively or may expose us to legal and regulatory risk by not adhering to regulatory requirements and restrictions governing the sale and promotion of prescription drug therapeutics, including those restricting off-label promotion. If we do not establish commercialization capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing the therapeutic candidates within our Wholly Owned Pipeline, if approved.

Even if any current or future therapeutic candidate of ours receives regulatory clearance or approval, it may fail to achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success, in which case we may not generate significant revenues or become profitable.

We have never commercialized a therapeutic, and even if any current or future therapeutic candidate of ours is approved by the appropriate regulatory authorities for marketing and sale, it may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. Physicians may be reluctant to take their patients off their current medications and switch their treatment regimen. Further, patients often acclimate to the treatment regime that they are currently taking and do not want to switch unless their physicians recommend switching therapeutics or they are required to switch due to lack of coverage and adequate reimbursement. In addition, even if we are able to demonstrate our Wholly Owned Programs' safety and efficacy to the FDA and other regulators, safety or efficacy concerns in the medical community may hinder market acceptance.

Efforts to educate the medical community and third-party payors on the benefits of the therapeutic candidates within our Wholly Owned Pipeline may require significant resources, including management time and financial resources, and may not be successful. The degree of market acceptance of the therapeutic candidates within our Wholly Owned Pipeline, if approved for commercial sale, will depend on a number of factors, including:

- the efficacy and safety of the therapeutic;
- the potential advantages of the therapeutic compared to competitive therapies;
- the prevalence and severity of any side effects;
- whether the therapeutic is designated under physician treatment guidelines as a first-, second- or third-line therapy;
- our ability, or the ability of any future collaborators, to offer the therapeutic for sale at competitive prices;
- the therapeutic's convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try, and of physicians to prescribe, the therapeutic;
- limitations or warnings, including distribution or use restrictions contained in the therapeutic's approved labelling;
- the strength of sales, marketing and distribution support;
- changes in the standard of care for the targeted indications for the therapeutic; and
- availability and adequacy of coverage and reimbursement from government payors, managed care plans and other third-party payors.

Sales of medical therapeutics also depend on the willingness of physicians to prescribe the treatment, which is likely to be based on a determination by these physicians that the therapeutics are safe, therapeutically effective and cost effective. In addition, the inclusion or exclusion of therapeutics from treatment guidelines established by various physician groups and the viewpoints of influential physicians can affect the willingness of other physicians to prescribe the treatment. We cannot predict whether physicians, physicians' organizations, hospitals, other healthcare providers, government agencies or private insurers will determine that our therapeutic is safe, therapeutically effective and cost effective as compared with competing treatments. If any therapeutic candidates we develop do not achieve an adequate level of acceptance, we may not generate significant therapeutic revenue, and we may not become profitable.

Any failure by any current or future therapeutic candidate of ours that obtains regulatory approval to achieve market acceptance or commercial success would adversely affect our business prospects. In addition, any negative perception of one of our Founded Entities or any therapeutic candidates marketed or commercialized by them may adversely affect our reputation in the marketplace or among industry participants and our business prospects.

The insurance coverage and reimbursement status of newly-approved therapeutics is uncertain. The therapeutic candidates within our Wholly Owned Pipeline may become subject to unfavorable pricing regulations, third-party coverage and reimbursement practices, or healthcare reform initiatives, which would harm our business. Failure to obtain or maintain coverage and adequate reimbursement for new or current therapeutics could limit our ability to market those therapeutics and decrease our ability to generate revenue.

The regulations that govern marketing approvals, pricing, coverage, and reimbursement for new drugs and other medical therapeutics vary widely from country to country. In the United States, healthcare reform legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. Some countries require approval of the sale price of a therapeutic before it can

be marketed. In many countries, the pricing review period begins after marketing or therapeutic licensing approval is granted. In some foreign markets, pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a therapeutic in a particular country, but then be subject to price regulations that delay our commercial launch of the therapeutic, possibly for lengthy time periods, and negatively impact the revenue we are able to generate from the sale of the therapeutic in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more therapeutics or therapeutic candidates, even if any therapeutic candidates we may develop obtain marketing approval.

Our ability to successfully commercialize our therapeutics and therapeutic candidates also will depend in part on the extent to which coverage and adequate reimbursement for these therapeutics and related treatments will be available from government health administration authorities, private health insurers, and other organizations. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. The availability of coverage and extent of reimbursement by governmental and private payors is essential for most patients to be able to afford treatments such as gene therapy therapeutics. Sales of these or other therapeutic candidates that we may identify will depend substantially, both domestically and abroad, on the extent to which the costs of the therapeutic candidates within our Wholly Owned Pipeline will be paid by health maintenance, managed care, pharmacy benefit and similar healthcare management organizations, or reimbursed by government health administration authorities, private health coverage insurers and other third-party payors. If coverage and adequate reimbursement is not available, or is available only to limited levels, we may not be able to successfully commercialize our therapeutics or therapeutic candidates. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish or maintain pricing sufficient to realize a sufficient return on our investment. A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. In many countries, the prices of medical therapeutics are subject to varying price control mechanisms as part of national health systems. In general, the prices of medicines under such systems are substantially lower than in the United States. Other countries allow companies to fix their own prices for medicines, but monitor and control company profits. Additional foreign price controls or other changes in pricing regulation could restrict the amount that we are able to charge for the therapeutic candidates within our Wholly Owned Pipeline. Accordingly, in markets outside the United States, the reimbursement for therapeutics may be reduced compared with the United States and may be insufficient to generate commercially reasonable revenues and profits.

There is also significant uncertainty related to the insurance coverage and reimbursement of newly approved therapeutics and coverage may be more limited than the purposes for which the medicine is approved by the FDA or comparable foreign regulatory authorities. In the United States, the principal decisions about reimbursement for new medicines are typically made by the Centers for Medicare & Medicaid Services, or CMS, an agency within the U.S. Department of Health and Human Services. CMS decides whether and to what extent a new medicine will be covered and reimbursed under Medicare and private payors tend to follow CMS to a substantial degree. No uniform policy of coverage and reimbursement for therapeutics exists among third-party payors and coverage and reimbursement levels for therapeutics can differ significantly from payor to payor. As a result, the coverage determination process is often a time consuming and costly process that may require us to provide scientific and clinical support for the use of our therapeutics to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. It is difficult to predict what CMS will decide with respect to reimbursement for fundamentally novel therapeutics such as ours, as there is no body of established practices and precedents for these new therapeutics. Reimbursement agencies in Europe may be more conservative than CMS. For example, a number of cancer drugs have been approved for reimbursement in the United States and have not been approved for reimbursement in certain European countries. Moreover, eligibility for reimbursement does not imply that any drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale, and distribution. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs and may be incorporated into existing payments for other services. Our inability to promptly obtain coverage and profitable payment rates from both government-funded and private payors for any approved therapeutics we may develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize therapeutic candidates, and our overall financial condition. As noted above, in the United States we plan to have various programs to help patients afford our therapeutics, including patient assistance programs and co-pay coupon programs for eligible patients.

Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Our inability to promptly obtain coverage and profitable reimbursement rates third-party payors for any approved therapeutics that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize therapeutics and our overall financial condition.

Increasingly, third-party payors are requiring that pharmaceutical companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical therapeutics. We cannot be sure that reimbursement will be available for any therapeutic candidate that we commercialize and, if reimbursement is available, the level of reimbursement. Reimbursement may impact the demand for, or the price of, any therapeutic or therapeutic candidate for which we obtain marketing approval. In order to obtain reimbursement, physicians may need to show that patients have superior treatment outcomes with our therapeutics compared to standard of care drugs, including lower-priced generic versions of standard of care drugs. We expect to experience pricing pressures in connection with the sale of any of the therapeutic candidates within our Wholly Owned Pipeline, due to the trend toward managed healthcare, the increasing influence of health maintenance organizations and additional legislative changes. The downward pressure on healthcare costs in general, particularly prescription drugs and surgical procedures and other treatments, has become very intense. As a result, increasingly high barriers are being erected to the entry of new therapeutics. Additionally, we may develop companion diagnostic tests for use with our Wholly Owned Programs or our Founded Entities' therapeutic candidates. We, or our Founded Entities or our collaborators may be required to obtain coverage and reimbursement for these tests separate and apart from the coverage and reimbursement we seek for our Wholly Owned Programs or our Founded Entities' therapeutic candidates, once approved. Even if we or our Founded Entities obtain regulatory approval or clearance for such companion diagnostics, there is significant uncertainty regarding our ability to obtain coverage and adequate reimbursement for the same reasons applicable to our Wholly Owned Programs or our Founded Entities' therapeutic candidates. Medicare reimbursement methodologies, whether under Part A, Part B, or clinical laboratory fee schedule may be amended from time to time, and we cannot predict what effect any change to these methodologies would have on any therapeutic candidate or companion diagnostic for which we receive approval.

We have no sales, distribution, or marketing capabilities, and may invest significant financial and management resources to establish these capabilities. If we are unable to establish such capabilities or enter into agreements with third parties to market and sell our future therapeutics, if approved, we may be unable to generate any revenues.

Given our stage of development, we have no sales, distribution, or marketing capabilities. To successfully commercialize any therapeutics that may result from our development programs, we will need to develop sales and marketing capabilities in the United States, Europe, and other regions, either on our own or with others. We may enter into strategic alliances with other entities to utilize their mature marketing and distribution capabilities, but we may be unable to enter into marketing agreements on favorable terms, if at all. If our future strategic collaborators do not commit sufficient resources to commercialize our future therapeutics, if any, and we are unable to develop the necessary marketing capabilities on our own, we may be unable to generate sufficient therapeutic revenue to sustain our business. We will be competing with many companies that currently have extensive and well-funded marketing and sales operations. Without a significant internal team or the support of a third party to perform marketing and sales functions, we may be unable to compete successfully against these more established companies.

Risks Related to Compliance with Healthcare Laws

If we fail to comply with healthcare laws, we could face substantial penalties and our business, operations and financial conditions could be adversely affected.

Healthcare providers, physicians and third-party payors in the United States and elsewhere play a primary role in the recommendation and prescription of pharmaceutical therapeutics. Arrangements with healthcare providers, third-party payors and customers can expose pharmaceutical manufacturers to broadly applicable fraud and abuse and other healthcare laws and regulations, including, without limitation, the federal Anti-Kickback Statute and the federal False Claims Act, or the FCA, which may constrain the business or financial arrangements and relationships through which such companies sell, market and distribute pharmaceutical therapeutics. In particular, the promotion, sales and marketing of healthcare items

and services, as well as certain business arrangements in the healthcare industry, are subject to extensive laws designed to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of ownership, pricing, discounting, marketing and promotion, structuring and commission(s), certain customer incentive programs and other business arrangements generally. Activities subject to these laws also involve the improper use of information obtained in the course of patient recruitment for clinical trials. The applicable federal and state healthcare laws and regulations laws that may affect our ability to operate include, but are not limited to:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, receiving, offering or paying any remuneration (including any kickback, bribe, or rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce, or in return for, either the referral of an individual, or the purchase, lease, order or recommendation of any good, facility, item or service for which payment may be made, in whole or in part, under a federal healthcare program, such as the Medicare and Medicaid programs. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. Violations are subject to civil and criminal fines and penalties for each violation, plus up to three times the remuneration involved, imprisonment of up to ten years, and exclusion from government healthcare programs. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the FCA. The Anti-Kickback Statute has been interpreted to apply to arrangements between pharmaceutical manufacturers, on the one hand, and prescribers, purchasers and formulary managers, on the other. There are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution. On December 2, 2020, the Office of Inspector General, or OIG, published further modifications to the federal Anti-Kickback Statute. Under the final rules, OIG added safe harbor protections under the Anti-Kickback Statute for certain coordinated care and value-based arrangements among clinicians, providers, and others. This rule (with exceptions) became effective January 19, 2021. Implementation of this change and new safe harbors for point-of-sale reductions in price for prescription pharmaceutical therapeutics and pharmacy benefit manager service fees are currently under review by the Biden administration and may be amended or repealed. We continue to evaluate what effect, if any, the rule will have on our business
- federal civil and criminal false claims laws and civil monetary penalty laws, including the False Claims Act, which impose criminal and civil penalties, including through civil "qui tam" or "whistleblower" actions, against individuals or entities for, among other things, knowingly presenting, or causing to be presented, claims for payment or approval from Medicare, Medicaid, or other federal health care programs that are false or fraudulent; knowingly making or causing a false statement material to a false or fraudulent claim or an obligation to pay money to the federal government; or knowingly concealing or knowingly and improperly avoiding or decreasing such an obligation. Manufacturers can be held liable under the FCA even when they do not submit claims directly to government payors if they are deemed to "cause" the submission of false or fraudulent claims. The FCA also permits a private individual acting as a "whistleblower" to bring actions on behalf of the federal government alleging violations of the FCA and to share in any monetary recovery. When an entity is determined to have violated the federal civil False Claims Act, the government may impose civil fines and penalties for each false claim, plus treble damages, and exclude the entity from participation in Medicare, Medicaid and other federal healthcare programs;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created additional federal criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e.g., public or private) and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false statements in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare matters. Similar to the federal Anti-Kickback Statute, a person or entity can be found guilty of violating HIPAA without actual knowledge of the statute or specific intent to violate it;
- the federal civil monetary penalties laws, which impose civil fines for, among other things, the offering or transfer or remuneration to a Medicare or state healthcare program beneficiary if the person knows or should know it is likely to influence the beneficiary's selection of a particular provider, practitioner, or supplier of services reimbursable by Medicare or a state healthcare program, unless an exception applies;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and their respective implementing regulations, which impose, among other things, requirements on certain covered healthcare providers, health plans, and healthcare clearinghouses as well as their respective business associates that perform services for them that involve the use, or disclosure of, individually identifiable health information, relating to the privacy, security and transmission of individually identifiable health information without appropriate authorization. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys' fees and costs associated with pursuing federal civil actions;
- the federal Physician Payments Sunshine Act, created under the ACA, and its implementing regulations, which require manufacturers of drugs, devices, biologicals and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report annually to the U.S. Department of Health and Human Services, or HHS, under the Open Payments Program, information related to payments or other transfers of value made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Effective January 1, 2022, these reporting obligations will extend to include transfers of value made to certain non-physician providers such as physician assistants and nurse practitioners;
- federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers;
- federal price reporting laws, which require manufacturers to calculate and report complex pricing metrics to government programs, where such reported prices may be used in the calculation of reimbursement and/or discounts on approved therapeutics; and
- analogous state and foreign laws and regulations, such as state and foreign anti-kickback, false claims, consumer protection and unfair competition laws which may apply to pharmaceutical business practices, including but not limited to, research, distribution, sales and marketing arrangements as well as submitting claims involving healthcare items or services reimbursed by any third-party payer, including commercial insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government that otherwise restricts payments that may be made to healthcare providers and other potential referral sources; state laws that require drug manufacturers to file reports with states regarding pricing and marketing information, such as the tracking and reporting of gifts, compensations and other remuneration and items of value provided to healthcare professionals and entities; state and local laws requiring the registration of pharmaceutical sales representatives; and state and foreign laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and are often not pre-empted by HIPAA, thus complicating compliance efforts.

Because of the breadth of these laws and the narrowness of the statutory exceptions and regulatory safe harbors available, it is possible that some of our business activities, including compensation of physicians with stock or stock options, could, despite efforts to comply, be subject to challenge under one or more of such laws. Additionally, FDA or foreign regulators may not agree that we have mitigated any risk of bias in our clinical trials due to payments or equity interests provided to investigators or institutions which could limit a regulator's acceptance of those clinical trial data in support of a marketing application. Moreover, efforts to ensure that our business arrangements will comply with applicable healthcare laws may involve substantial costs. It is possible that governmental and enforcement authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law interpreting applicable fraud and abuse or other healthcare laws and regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant civil, criminal and administrative penalties, damages, disgorgement, monetary fines, exclusion from participation in Medicare, Medicaid and other federal healthcare programs, integrity and oversight agreements to resolve allegations of non-compliance, contractual damages, reputational harm, diminished profits and future earnings, and curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations. In addition, the approval and commercialization of any of the therapeutic candidates within our Wholly Owned Pipeline outside the United States will also likely subject us to foreign equivalents of the healthcare laws mentioned above, among other foreign laws.

Failure to comply with health and data protection laws and regulations could lead to government enforcement actions (which could include civil or criminal penalties), private litigation, and/or adverse publicity and could negatively affect our operating results and business.

We and any potential collaborators may be subject to federal, state, and foreign data protection laws and regulations (i.e., laws and regulations that address privacy and data security). In the United States, numerous federal and state laws and regulations, including federal health information privacy laws, state data breach notification laws, state health information privacy laws, and federal and state consumer protection laws (e.g., Section 5 of the Federal Trade Commission Act), that govern the collection, use, disclosure and protection of health-related and other personal information could apply to our operations or the operations of our collaborators. In addition, we may obtain health information from third parties (including research institutions from which we obtain clinical trial data) that are subject to privacy and security requirements under HIPAA, as amended by HITECH. Depending on the facts and circumstances, we could be subject to civil, criminal, and administrative penalties if we knowingly obtain, use, or disclose individually identifiable health information maintained by a HIPAA-covered entity in a manner that is not authorized or permitted by HIPAA.

Compliance with U.S. and international data protection laws and regulations, including the General Data Protection Regulation 2016/679, or GDPR, in the European Union, could require us to take on more onerous obligations in our contracts, restrict our ability to collect, use and disclose data, or in some cases, impact our ability to operate in certain jurisdictions. Failure to comply with these laws and regulations could result in government enforcement actions (which could include civil, criminal and administrative penalties), private litigation, and/or adverse publicity and could negatively affect our operating results and business. Moreover, clinical trial subjects, employees and other individuals about whom we or our potential collaborators obtain personal information, as well as the providers who share this information with us, may limit our ability to collect, use and disclose the information. Claims that we have violated individuals' privacy rights, failed to comply with data protection laws, or breached our contractual obligations, even if we are not found liable, could be expensive and time-consuming to defend and could result in adverse publicity that could harm our business.

Healthcare legislative measures aimed at reducing healthcare costs may have a material adverse effect on our business and results of operations.

The United States and many foreign jurisdictions have enacted or proposed legislative and regulatory changes affecting the healthcare system that could prevent or delay marketing approval of the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates or any future therapeutic candidates, restrict or regulate post-approval activities and affect our or our Founded Entities' ability to profitably sell any therapeutic for which we or our Founded Entities obtain marketing approval. Changes in regulations, statutes or the interpretation of existing regulations could impact our or our Founded Entities' business in the future by requiring, for example: (i) changes to our manufacturing arrangements; (ii) additions or modifications to therapeutic labeling; (iii) the recall or discontinuation of our therapeutics; or (iv) additional record-keeping requirements. If any such changes were to be imposed, they could adversely affect the operation of our business.

In the United States, there have been and continue to be a number of legislative initiatives and judicial challenges to contain healthcare costs. For example, in March 2010, the Affordable Care Act, or the ACA, was passed, which substantially changed the way healthcare is financed by both governmental and private insurers, and significantly impacted the U.S. pharmaceutical industry. The ACA, among other things, subjects biological therapeutics to potential competition by lower-cost biosimilars, addresses a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected, increases the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extends the rebate program to individuals enrolled in Medicaid managed care organizations, establishes annual fees and taxes on manufacturers of certain branded prescription drugs, and creates a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 70 percent point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D.

Payment methodologies may be subject to changes in healthcare legislation and regulatory challenges. For example, in order for a drug therapeutic to receive federal reimbursement under the Medicaid or Medicare Part B programs or to be sold directly to U.S. government agencies, the manufacturer must extend discounts to entities eligible to participate in the 340B drug pricing program. In December 2018, the CMS published a final rule permitting further collections and payments to and from certain ACA qualified health plans and health insurance issuers under the ACA risk adjustment program in response to the outcome of the federal district court litigation regarding the method CMS uses to determine this risk adjustment. Since then, the ACA risk adjustment program payment parameters have been updated annually.

Since the enactment of the ACA, there have been numerous judicial, administrative, executive, and legislative challenges to certain aspects of the ACA, and we expect there will be additional challenges and amendments to the ACA in the future. The Tax Cuts and Jobs Act of 2017, or the Tax Act, includes a provision that repealed effective January 1, 2019 the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate." On December 14, 2018, a U.S. District Court Judge in the Northern District of Texas, or the Texas District Court Judge, ruled that the individual mandate is a critical and inseverable feature of the ACA, and therefore, because it was repealed as part of the Tax Act, the remaining provisions of the ACA are invalid as well. The former Trump Administration and CMS have both stated that the ruling will have no immediate effect, and on December 30, 2018 the Texas District Court Judge issued an order staying the judgment pending appeal. On December 18, 2019, the U.S. Court of Appeals for the 5th Circuit ruled that the individual mandate was unconstitutional but remanded the case back to the District Court to determine whether the remaining provisions of the ACA are invalid as well. On March 2, 2020, the U.S. Supreme Court granted the petitions for writs of certiorari to review the case, and held oral arguments on November 10, 2020. Pending a decision, the ACA remains in effect, but it is unclear at this time what effect these developments will have on the status of the ACA. We will continue to evaluate the effect that the ACA and its possible repeal and replacement has on our business.

Since January 2017, former President Trump signed various Executive Orders designed to delay the implementation of certain provisions of the ACA or otherwise circumvent some of the requirements for health insurance mandated by the ACA. On October 13, 2017, former President Trump signed an Executive Order terminating the cost-sharing subsidies that reimburse insurers under the ACA. The former Trump administration concluded that cost-sharing reduction, or CSR, payments to insurance companies required under the ACA have not received necessary appropriations from Congress and announced that it would discontinue these payments immediately until those appropriations are made. Several state Attorneys General filed suit to stop the administration from terminating the subsidies, but their request for a restraining order was denied by a federal judge in California on October 25, 2017. On August 14, 2020, the U.S. Court of Appeals for the Federal Circuit ruled in two separate cases that the federal government is liable for the full amount of unpaid CSRs for the years preceding and including 2017. For CSR claims made by health insurance companies for years 2018 and later, further litigation will be required to determine the amounts due, if any. Further, on June 14, 2018, U.S. Court of Appeals for the Federal Circuit ruled that the federal government was not required to pay more than $12 billion in ACA risk corridor payments to third-party payors who argued were owed to them. This decision was appealed to the U.S. Supreme Court, which on April 27, 2020, reversed the U.S. Court of Appeals for the Federal Circuit's decision and remanded the case to the U.S. Court of Federal Claims, concluding the government has an obligation to pay these risk corridor payments under the relevant formula. The U.S. federal government has since started sending third-party payors owed payments. It is not clear what effect these rulings will have on our business, but we will continue to monitor any developments.

Moreover, on January 22, 2018, former President Trump signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain ACA-mandated fees, including the so called "Cadillac" tax on certain high cost employer-sponsored insurance plans, the annual fee imposed on certain health insurance providers based on market share, and the medical device excise tax on non-exempt medical devices. However, on December 20, 2019, the U.S. President signed into law the Further Consolidated Appropriations Act (H.R. 1865), which repeals the Cadillac tax, the health insurance provider tax, and the medical device excise tax. The Bipartisan Budget Act of 2018, also amended the ACA, effective January 1, 2019, by increasing the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D and closing the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole." In addition, CMS published a final rule on April 25, 2019 that gave states greater flexibility, starting in 2020, in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the ACA for plans sold through such marketplaces.

In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, resulted in aggregate reductions of Medicare payments to providers of 2 percent per fiscal year, which went into effect in 2013, and, due to subsequent legislative amendments, will remain in effect through 2030 unless additional Congressional action is taken. However, pursuant to the Coronavirus Aid, Relief and Economic

Security Act, or CARES Act, and due to subsequent legislation, these Medicare sequester reductions were suspended from May 1, 2020 through March 31, 2021 due to the COVID-19 pandemic. Proposed legislation, if passed, would extend this suspension until the end of the pandemic. The American Taxpayer Relief Act of 2012 further reduced Medicare payments to several types of providers, including hospitals and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

There has been increasing legislative and enforcement interest in the United States with respect to drug pricing practices. Specifically, there have been several recent U.S. Congressional inquiries and proposed federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. At the federal level, the former Trump administration's budget for fiscal year 2021 includes a $135 billion allowance to support legislative proposals seeking to reduce drug prices, increase competition, lower out-of-pocket drug costs for patients, and increase patient access to lower-cost generic and biosimilar drugs. On March 10, 2020, the former Trump administration sent "principles" for drug pricing to Congress, calling for legislation that would, among other things, cap Medicare Part D beneficiary out-of-pocket pharmacy expenses, provide an option to cap Medicare Part D beneficiary monthly out-of-pocket expenses, and place limits on pharmaceutical price increases. Additionally, the former Trump administration released a "Blueprint" to lower drug prices and reduce out of pocket costs of drugs that contains additional proposals to increase manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their therapeutics and reduce the out of pocket costs of drug therapeutics paid by consumers. The U.S. Department of HHS has already started the process of soliciting feedback on some of these measures and, at the same time, is immediately implementing others under its existing authority. For example, in May 2019, CMS issued a final rule to allow Medicare Advantage Plans the option of using step therapy for Part B drugs beginning January 1, 2020. This final rule codified CMS's policy change that was effective January 1, 2019. However, it is unclear whether the Biden administration will challenge, reverse, revoke or otherwise modify these executive and administrative actions.

In addition, on May 30, 2018, the Right to Try Act was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational new drug therapeutics that have completed a Phase 1 clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a drug manufacturer to make its drug therapeutics available to eligible patients as a result of the Right to Try Act.

In 2020, former President Trump announced several executive orders related to prescription drug pricing that seek to implement several of the administration's proposals. The FDA released a final rule on September 24, 2020, which went into effect on November 30, 2020, providing guidance for states to build and submit importation plans for drugs from Canada. Further, on November 20, 2020, CMS issued an Interim Final Rule implementing the Most Favored Nation, or MFN, Model under which Medicare Part B reimbursement rates will be calculated for certain drugs and biologicals based on the lowest price drug manufacturers receive in Organization for Economic Cooperation and Development countries with a similar gross domestic product per capita. The MFN Model regulations mandate participation by identified Part B providers and would have applied to all U.S. states and territories for a seven-year period beginning January 1, 2021, and ending December 31, 2027. However, in response to a lawsuit filed by several industry groups, on December 28, the U.S. District Court for the Northern District of California issued a nationwide preliminary injunction enjoining government defendants from implementing the MFN Rule pending completion of notice-and-comment procedures under the Administrative Procedure Act. On January 13, 2021, in a separate lawsuit brought by industry groups in the U.S. District of Maryland, the government defendants entered a joint motion to stay litigation on the condition that the government would not appeal the preliminary injunction granted in the U.S. District Court for the Northern District of California and that performance for any final regulation stemming from the MFN Interim Final Rule shall not commence earlier than 60 days after publication of that regulation in the Federal Register. Further, authorities in Canada have passed rules designed to safeguard the Canadian drug supply from shortages. If implemented, importation of drugs from Canada and the MFN Model may materially and adversely affect the price we receive for any of our therapeutic candidates. Additionally, on December 2, 2020, HHS published a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers. Pursuant to an order entered by the U.S. District Court for the District of Columbia, the portion of the rule eliminating safe harbor protection for certain rebates related to the sale or purchase of a pharmaceutical therapeutic from a manufacturer to a plan sponsor under Medicare Part D has been delayed to January 1, 2023. Further, implementation of this change and new safe harbors for point-of-sale reductions in price for prescription pharmaceutical therapeutics and pharmacy benefit manager service fees are currently under review by the Biden administration and may be amended or repealed.

At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological therapeutic pricing, including price or patient reimbursement constraints, discounts, restrictions on certain therapeutic access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical therapeutics and which suppliers will be included in their prescription drug and other healthcare programs. Furthermore, there has been increased interest by third-party payors and governmental authorities in reference pricing systems and publication of discounts and list prices.

There have been, and likely will continue to be, legislative and regulatory proposals at the foreign, federal and state levels directed at containing or lowering the cost of healthcare. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our therapeutic. Such reforms could have an adverse effect on anticipated revenue from therapeutic candidates that we may successfully develop and for which we may obtain regulatory approval and may affect our overall financial condition and ability to develop therapeutic candidates. We cannot predict the initiatives that may be adopted in the future. The continuing efforts of the government, insurance companies, managed care organizations and other payors of healthcare services to contain or reduce costs of healthcare and/or impose price controls may adversely affect:

- the demand for the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates, if approved;
- our ability to receive or set a price that we believe is fair for our therapeutics;
- our ability to generate revenue and achieve or maintain profitability;
- the amount of taxes that we are required to pay; and
- the availability of capital.

Other healthcare reform measures may be adopted in the future, and may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, lower reimbursement, and new payment methodologies. This could lower the price that we receive for any approved therapeutic. Any denial in coverage or reduction in reimbursement from Medicare or other government-funded programs may result in a similar denial or reduction in payments from private payors, which may prevent us from being able to generate sufficient revenue, attain profitability or commercialize the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates, if approved. Litigation and legislative efforts to change or repeal the ACA are likely to continue, with unpredictable and uncertain results.

Risks Related to Competition

We face significant competition in an environment of rapid technological and scientific change, and there is a possibility that our competitors may achieve regulatory approval before us or develop therapies that are safer, more advanced or more effective than ours, which may negatively impact our ability to successfully market or commercialize any therapeutic candidates we may develop and ultimately harm our financial condition.

The development and commercialization of new drug therapeutics is highly competitive. We may face competition with respect to any therapeutic candidates that we seek to develop or commercialize in the future from major pharmaceutical companies, specialty pharmaceutical companies, and biotechnology companies worldwide. Potential competitors also include academic institutions, government agencies, and other public and private research organizations that conduct research, seek patent protection, and establish collaborative arrangements for research, development, manufacturing, and commercialization.

There are a number of major pharmaceutical and biotechnology companies that are currently pursuing the development and commercialization of potential medicines targeting similar treatment areas as we are. If any of our competitors receive FDA approval before we do, the therapeutic candidates within our Wholly Owned Pipeline would not be the first

treatment on the market, and our market share may be limited. In addition to competition from other companies targeting our target indications, any therapeutics we may develop may also face competition from other types of therapies.

Many of our current or potential competitors, either alone or with their strategic partners, have:

- greater financial, technical, and human resources than we have at every stage of the discovery, development, manufacture, and commercialization of therapeutics;
- more extensive resources for preclinical testing, conducting clinical trials, obtaining regulatory approvals, and in manufacturing, marketing, and selling drug therapeutics;
- therapeutics that have been approved or are in late stages of development; and
- collaborative arrangements in our target markets with leading companies and research institutions.

Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize therapeutics that are safer, more effective, have fewer or less severe side effects, are more convenient, or are less expensive than any therapeutics that we may develop. Furthermore, currently approved therapeutics could be discovered to have application for treatment of our targeted disease indications or similar indications, which could give such therapeutics significant regulatory and market timing advantages over the therapeutic candidates within our Wholly Owned Pipeline. Our competitors may also obtain FDA, EMA or other comparable foreign regulatory approval for their therapeutics more rapidly than we may obtain approval for ours and may obtain orphan therapeutic exclusivity from the FDA for indications that we are targeting, which could result in our competitors establishing a strong market position before we are able to enter the market. Additionally, therapeutics or technologies developed by our competitors may render our potential therapeutic candidates uneconomical or obsolete and we may not be successful in marketing any therapeutic candidates we may develop against competitors.

In addition, we could face litigation or other proceedings with respect to the scope, ownership, validity and/or enforceability of our patents relating to our competitors' therapeutics and our competitors may allege that our therapeutics infringe, misappropriate or otherwise violate their intellectual property. The availability of our competitors' therapeutics could limit the demand, and the price we are able to charge, for any therapeutics that we may develop and commercialize.

The therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates for which we or our Founded Entities intend to seek approval as biologic therapeutics may face competition sooner than anticipated.

If we or our Founded Entities are successful in achieving regulatory approval to commercialize any biologic therapeutic candidate we or our Founded Entities develop alone or with collaborators, it may face competition from biosimilar therapeutics. In the United States, certain of the therapeutic candidates within our Wholly Owned Pipeline and our Founded Entities' therapeutic candidates are regulated by the FDA as biologic therapeutics subject to approval under the BLA pathway. The Biologics Price Competition and Innovation Act of 2009, or BPCIA, created an abbreviated pathway for the approval of biosimilar and interchangeable biologic therapeutics following the approval of an original BLA. The abbreviated regulatory pathway establishes legal authority for the FDA to review and approve biosimilar biologics, including the possible designation of a biosimilar as "interchangeable" based on its similarity to an existing brand therapeutic. Under the BPCIA, an application for a biosimilar therapeutic may not be submitted until four years following the date that the reference therapeutic was first licensed by the FDA. In addition, the approval of a biosimilar therapeutic may not be made effective by the FDA until 12 years after the reference therapeutic was first licensed by the FDA. During this 12-year period of exclusivity, another company may still market a competing version of the reference therapeutic if the FDA approves a full BLA for the competing therapeutic containing the sponsor's own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of their therapeutic.

We believe that any of the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates that are approved as a biological therapeutic under a BLA should qualify for the 12-year period of exclusivity. However, there is a risk that this exclusivity could be shortened due to congressional action or otherwise, or that the FDA will not consider such therapeutic candidates to be reference therapeutics for competing therapeutics, potentially creating the opportunity for generic competition sooner than anticipated. Other aspects of the BPCIA, some of which may impact the BPCIA exclusivity provisions, have also been the subject of recent litigation. Moreover, the extent to which a biosimilar therapeutic, once approved, will be substituted for any one of our, our Founded Entities' or our collaborators' reference therapeutics in a way that is similar to traditional generic substitution for non-biologic therapeutics is not yet clear, and will depend on a number of marketplace and regulatory factors that are still developing. If competitors are able to obtain marketing approval for biosimilars referencing any therapeutics that we or our Founded Entities develop alone or with collaborators that may be approved, such therapeutics may become subject to competition from such biosimilars, with the attendant competitive pressure and potential adverse consequences.

Risks Related to Reliance on Third Parties

We are currently party to and may seek to enter into additional collaborations, licenses and other similar arrangements and may not be successful in maintaining existing arrangements or entering into new ones, and even if we are, we may not realize the benefits of such relationships.

We are currently parties to license and collaboration agreements with a number of universities and pharmaceutical companies and expect to enter into additional agreements as part of our business strategy. The success of our current and any future collaboration arrangements will depend heavily on the efforts and activities of our collaborators. Collaborations are subject to numerous risks, which may include risks that:

- collaborators may have significant discretion in determining the efforts and resources that they will apply to collaborations;
- collaborators may not pursue development and commercialization of the therapeutic candidates within our Wholly Owned Pipeline or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in their strategic focus due to their acquisition of competitive therapeutics or their internal development of competitive therapeutics, availability of funding or other external factors, such as a business combination that diverts resources or creates competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial, abandon a therapeutic candidate, repeat or conduct new clinical trials or require a new formulation of a therapeutic candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, therapeutics that compete directly or indirectly with our therapeutics or therapeutic candidates;
- a collaborator with marketing, manufacturing and distribution rights to one or more therapeutics may not commit sufficient resources to or otherwise not perform satisfactorily in carrying out these activities;
- we could grant exclusive rights to our collaborators that would prevent us from collaborating with others;
- collaborators may not properly maintain or defend our intellectual property rights or may use our intellectual property or proprietary information in a way that gives rise to actual or threatened litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential liability;
- disputes may arise between us and a collaborator that cause the delay or termination of the research, development or commercialization of our current or future therapeutic candidates or that results in costly litigation or arbitration that diverts management attention and resources;
- collaborations may be terminated, which may result in a need for additional capital to pursue further development or commercialization of the applicable current or future therapeutic candidates;
- collaborators may own or co-own intellectual property covering therapeutics that result from our collaboration with them, and in such cases, we would not have the exclusive right to develop or commercialize such intellectual property;
- disputes may arise with respect to the ownership of any intellectual property developed pursuant to our collaborations; and
- a collaborator's sales and marketing activities or other operations may not be in compliance with applicable laws resulting in civil or criminal proceedings.

Additionally, we may seek to enter into additional collaborations, joint ventures, licenses and other similar arrangements for the development or commercialization of the therapeutic candidates within our Wholly Owned Pipeline, due to capital costs required to develop or commercialize the therapeutic candidate or manufacturing constraints. We may not be successful in our efforts to establish such collaborations for the therapeutic candidates within our Wholly Owned Pipeline because our R&D pipeline may be insufficient, the therapeutic candidates within our Wholly Owned

Pipeline may be deemed to be at too early of a stage of development for collaborative effort or third parties may not view the therapeutic candidates within our Wholly Owned Pipeline as having the requisite potential to demonstrate safety and efficacy or significant commercial opportunity. In addition, we face significant competition in seeking appropriate strategic partners, and the negotiation process can be time consuming and complex. Further, any future collaboration agreements may restrict us from entering into additional agreements with potential collaborators. We cannot be certain that, following a strategic transaction or license, we will achieve an economic benefit that justifies such transaction.

Even if we are successful in our efforts to establish such collaborations, the terms that we agree upon may not be favorable to us, and we may not be able to maintain such collaborations if, for example, development or approval of a therapeutic candidate is delayed, the safety of a therapeutic candidate is questioned or sales of an approved therapeutic candidate are unsatisfactory.

In addition, any potential future collaborations may be terminable by our strategic partners, and we may not be able to adequately protect our rights under these agreements. Furthermore, strategic partners may negotiate for certain rights to control decisions regarding the development and commercialization of the therapeutic candidates within our Wholly Owned Pipeline, if approved, and may not conduct those activities in the same manner as we do. Any termination of collaborations we enter into in the future, or any delay in entering into collaborations related to the therapeutic candidates within our Wholly Owned Pipeline, could delay the development and commercialization of the therapeutic candidates within our Wholly Owned Pipeline and reduce their competitiveness if they reach the market, which could have a material adverse effect on our business, financial condition and results of operations.

Collaborative relationships with third parties could cause us to expend significant resources and give rise to substantial business risk with no assurance of financial return.

We anticipate relying upon strategic collaborations for marketing and commercializing our existing therapeutic candidates, and we may rely even more on strategic collaborations for R&D of other therapeutic candidates or discoveries. We may sell therapeutic offerings through strategic partnerships with pharmaceutical and biotechnology companies. If we are unable to establish or manage such strategic collaborations on terms favorable to us in the future, our R&D efforts and potential to generate revenue may be limited.

If we enter into R&D collaborations during the early phases of therapeutic development, success will in part depend on the performance of research collaborators. We will not directly control the amount or timing of resources devoted by research collaborators to activities related to therapeutic candidates. Research collaborators may not commit sufficient resources to our R&D programs. If any research collaborator fails to commit sufficient resources, the preclinical or clinical development programs related to the collaboration could be delayed or terminated. Also, collaborators may pursue existing or other development-stage therapeutics or alternative technologies in preference to those being developed in collaboration with us. Finally, if we fail to make required milestone or royalty payments to collaborators or to observe other obligations in agreements with them, the collaborators may have the right to terminate or stop performance of those agreements.

Establishing strategic collaborations is difficult and time-consuming. Our discussions with potential collaborators may not lead to the establishment of collaborations on favorable terms, if at all. Potential collaborators may reject collaborations based upon their assessment of our financial, regulatory or intellectual property position. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators. Even if we successfully establish new collaborations, these relationships may never result in the successful development or commercialization of therapeutic candidates or the generation of sales revenue. To the extent that we enter into collaborative arrangements, the related therapeutic revenues are likely to be lower than if we directly marketed and sold therapeutics. Such collaborators may also consider alternative therapeutic candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us for any future therapeutic candidate.

Management of our relationships with collaborators will require:

- significant time and effort from our management team;
- coordination of our marketing and R&D programs with the marketing and R&D priorities of our collaborators; and
- effective allocation of our resources to multiple projects.

We rely on third parties to assist in conducting our clinical trials and some aspects of our research and preclinical testing, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials, research, or testing.

We currently rely and expect to continue to rely on third parties, such as CROs, clinical data management organizations, medical institutions, and clinical investigators, to conduct some aspects of research and preclinical testing and clinical trials. Any of these third parties may terminate their engagements with us or be unable to fulfill their contractual obligations. If any of our relationships with these third parties terminate, we may not be able to enter into arrangements with alternative third parties on commercially reasonable terms, or at all. If we need to enter into alternative arrangements, it would delay therapeutic development activities.

Further, although our reliance on these third parties for clinical development activities limits our control over these activities, we remain responsible for ensuring that each of our trials is conducted in accordance with the applicable protocol, legal and regulatory requirements and scientific standards. For example, notwithstanding the obligations of a CRO for a trial of one of the therapeutic candidates within our Wholly Owned Pipeline, we remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA requires us to comply with requirements, commonly referred to as GCPs, for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. The FDA enforces these GCPs through periodic inspections of trial sponsors, principal investigators, clinical trial sites and IRBs. If we or our third-party contractors fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA may require us to perform additional clinical trials before approving the therapeutic candidates within our Wholly Owned Pipeline, which would delay the regulatory approval process. We cannot be certain that, upon inspection, the FDA will determine that any of our clinical trials comply with GCPs. We are also required to register certain clinical trials and post the results of completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within certain timeframes. NIH and FDA recently signaled the government's willingness to begin enforcing those requirements against non-compliant clinical trial sponsors. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

Furthermore, the third parties conducting clinical trials on our behalf are not our employees, and except for remedies available to us under our agreements with such contractors, we cannot control whether or not they devote sufficient time, skill and resources to our ongoing development programs. These contractors may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other drug or medical device development activities, which could impede their ability to devote appropriate time to our clinical programs. If these third parties, including clinical investigators, do not successfully carry out their contractual duties, meet expected deadlines or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we may not be able to obtain, or may be delayed in obtaining, regulatory approvals for the therapeutic candidates within our Wholly Owned Pipeline. If that occurs, we will not be able to, or may be delayed in our efforts to, successfully commercialize the therapeutic candidates within our Wholly Owned Pipeline. In such an event, our financial results and the commercial prospects for any therapeutic candidates that we seek to develop could be harmed, our costs could increase and our ability to generate revenues could be delayed, impaired or foreclosed.

Our or our Founded Entities' use of third parties to manufacture the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates and other therapeutic candidates that we or our Founded Entities may develop for preclinical studies and clinical trials may increase the risk that we or our Founded Entities will not have sufficient quantities of our or our Founded Entities' therapeutic candidates, therapeutics, or necessary quantities of such materials on time or at an acceptable cost.

With respect to certain of the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates, we and certain of our Founded Entities do not currently have, nor do we plan to acquire, the infrastructure or capability internally to manufacture drug supplies for our ongoing clinical trials or any future clinical trials that we or our Founded Entities may conduct, and we and our Funded Entities lack the resources to manufacture any therapeutic candidates on a commercial scale. We rely, and expect to continue to rely, on third-party manufacturers to produce our and certain of our Founded Entities' therapeutic candidates or other therapeutic candidates that we or our Founded Entities may

identify for clinical trials, as well as for commercial manufacture if any therapeutic candidates receive marketing authorization. Although we and our Founded Entities generally do not begin a clinical trial unless we or our Founded Entities believe we have a sufficient supply of a therapeutic candidate to complete the trial, any significant delay or discontinuity in the supply of a therapeutic candidate, or the raw material components thereof, for an ongoing clinical trial due to the need to replace a third-party manufacturer could considerably delay the clinical development and potential regulatory authorization of the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates, which could harm our business and results of operations.

We or our Founded Entities may be unable to identify and appropriately qualify third-party manufacturers or establish agreements with third-party manufacturers or do so on acceptable terms. Even if we or our Founded Entities are able to establish agreements with third-party manufacturers, reliance on third-party manufacturers entails additional risks, including:

- reliance on the third party for sourcing of raw materials, components, and such other goods as may be required for execution of its manufacturing processes and the oversight by the third party of its suppliers;
- reliance on the third party for regulatory compliance and quality assurance for the manufacturing activities each performs;
- the possible breach of the manufacturing agreement by the third party;
- the possible misappropriation of proprietary information, including trade secrets and know-how; and
- the possible termination or non-renewal of the agreement by the third party at a time that is costly or inconvenient for us or our Founded Entities.

Furthermore, all of our CMOs are engaged with other companies to supply and/or manufacture materials or therapeutics for such companies, which exposes our manufacturers to regulatory risks for the production of such materials and therapeutics. The facilities used by our contract manufacturers to manufacture our drug, or medical device therapeutic candidates are subject to review by the FDA pursuant to inspections that will be conducted after we submit an NDA, BLA, PMA application or other marketing application to the FDA. We do not control the manufacturing process of, and are to some extent dependent on, our contract manufacturing partners for compliance with the regulatory requirements, known as cGMP requirements for manufacture of drug, biologic and device therapeutics. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or others, we will not be able to secure or maintain regulatory authorization for the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates manufactured at these manufacturing facilities. In addition, we have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA, the EMA or another comparable foreign regulatory agency does not approve these facilities for the manufacture of the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates or if any agency withdraws its approval in the future, we or our Founded Entities may need to find alternative manufacturing facilities, which would negatively impact our or our Founded Entities' ability to develop, obtain regulatory authorization for or market the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates, if cleared or approved.

The therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates may compete with other therapeutic candidates and marketed therapeutics for access to manufacturing facilities. Any performance failure on the part of our or our Founded Entities' existing or future manufacturers could delay clinical development, marketing approval or commercialization. Our and certain of our Founded Entities' current and anticipated future dependence upon others for the manufacturing of the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates may adversely affect our future profit margins and our ability to commercialize any therapeutic candidates that receive marketing clearance or approval on a timely and competitive basis.

If the contract manufacturing facilities on which we and certain of our Founded Entities' rely do not continue to meet regulatory requirements or are unable to meet our or our Founded Entities' supply demands, our business will be harmed.

All entities involved in the preparation of therapeutic candidates for clinical trials or commercial sale, including our and certain of our Founded Entities' existing CMOs for the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates, are subject to extensive regulation. Components of a finished drug or biologic therapeutic approved for commercial sale or used in late-stage clinical trials must be manufactured in accordance with cGMP, or similar regulatory requirements outside the United States. These regulations govern manufacturing processes and procedures, including recordkeeping, and the implementation and operation of quality systems to control and assure the quality of investigational therapeutics and therapeutics approved for sale. Similarly, medical devices must be manufactured in accordance with QSR. Poor control of production processes can lead to the introduction of contaminants or to inadvertent changes in the properties or stability of Gelesis' Plenity, Akili's EndeavorRx, our Founded Entities' other therapeutic candidates or the therapeutic candidates within our Wholly Owned Pipeline. Our or our Founded Entities' failure, or the failure of third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us or our Founded Entities, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, suspension of production, seizures or recalls of therapeutic candidates or marketed drugs or devices, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect clinical or commercial supplies of the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates.

We and/or our CMOs must supply all necessary documentation, as applicable, in support of a marketing application, such as an NDA, BLA, PMA or MAA, on a timely basis and must adhere to regulations enforced by the FDA and other regulatory agencies through their facilities inspection program. Some of our CMOs have never produced a commercially approved pharmaceutical therapeutic and therefore have not obtained the requisite regulatory authority approvals to do so. The facilities and quality systems of some or all of our third-party contractors must pass a pre-approval inspection for compliance with the applicable regulations as a condition of regulatory approval of the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates or any of our other potential therapeutics. In addition, the regulatory authorities may, at any time, audit or inspect a manufacturing facility involved with the preparation of the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates or our other potential therapeutics or the associated quality systems for compliance with the regulations applicable to the activities being conducted. Although we oversee the CMOs, we cannot control the manufacturing process of, and are completely dependent on, our CMO partners for compliance with the regulatory requirements. If these facilities do not pass a pre-approval plant inspection, regulatory approval of the therapeutics may not be granted or may be substantially delayed until any violations are corrected to the satisfaction of the regulatory authority, if ever.

The regulatory authorities also may, at any time following clearance or approval of a therapeutic for sale, audit the manufacturing facilities of our third-party contractors. If any such inspection or audit identifies a failure to comply with applicable regulations or if a violation of our therapeutic specifications or applicable regulations occurs independent of such an inspection or audit, we or the relevant regulatory authority may require remedial measures that may be costly and/or time consuming for us or a third party to implement, and that may include the temporary or permanent suspension of a clinical study or commercial sales or the temporary or permanent closure of a facility. Any such remedial measures imposed upon us or third parties with whom we contract could materially harm our business.

Additionally, if supply from one approved manufacturer is interrupted, an alternative manufacturer would need to be qualified. For drug and biologic therapeutics, as applicable, an NDA, BLA supplement or MAA variation, or equivalent foreign regulatory filing, is also required, which could result in further delay. Similarly, for medical devices, a new marketing application or supplement may be required. The regulatory agencies may also require additional studies if a new manufacturer is relied upon for commercial production. Switching manufacturers may involve substantial costs and is likely to result in a delay in our desired clinical and commercial timelines.

These factors could cause us or our Founded Entities to incur higher costs and could cause the delay or termination of clinical trials, regulatory submissions, required approvals, or commercialization of the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates. Furthermore, if our or our Founded Entities' suppliers fail to meet contractual requirements and we or our Founded Entities are unable to secure one or more replacement suppliers capable of production at a substantially equivalent cost, our or our Founded Entities' clinical trials may be delayed or we or our Founded Entities could lose potential revenue.

Risks Related to Our Intellectual Property

Risks Related to Our Intellectual Property Protection

If we or our Founded Entities are unable to obtain and maintain sufficient intellectual property protection for our or our Founded Entities' existing therapeutic candidates or any other therapeutic candidates that we or they may identify, or if the scope of the intellectual property protection we or they currently have or obtain in the future is not sufficiently broad, our competitors could develop and commercialize therapeutic candidates similar or identical to ours, and our ability to successfully commercialize our existing therapeutic candidates and any other therapeutic candidates that we or they may pursue may be impaired.

As is the case with other pharmaceutical and biopharmaceutical companies, our success depends in large part on our ability to obtain and maintain protection of the intellectual property we may own solely and jointly with others, particularly patents, in the United States and other countries with respect to our Wholly Owned Programs or our Founded Entities' therapeutic candidates and technology. We and our Founded Entities seek to protect our proprietary position by filing patent applications in the United States and abroad related to our and our Founded Entities' existing therapeutic candidates, our various proprietary technologies, and any other therapeutic candidates or technologies that we or they may identify.

Obtaining, maintaining and enforcing pharmaceutical and biopharmaceutical patents is costly, time consuming and complex, and we may not be able to file or prosecute all necessary or desirable patent applications, or maintain, enforce or license patents that may issue from such patent applications, at a reasonable cost or in a timely manner. It is also possible that we could fail to identify patentable aspects of our R&D output before it is too late to obtain patent protection. Although we take reasonable measures, we have systems in place to remind us of filing and prosecution deadlines, and we employ outside firms and rely on outside counsel to monitor patent deadlines, we may miss or fail to meet a patent deadline, including in a foreign country, which could negatively impact our patent rights and harm our competitive position, business, and prospects. We may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the rights to patents licensed to third parties. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal, technological and factual questions and has in recent years been the subject of much litigation. The standards that the U.S. Patent and Trademark Office, or the USPTO, and its foreign counterparts use to grant patents are not always applied predictably or uniformly. In addition, the laws of foreign countries may not protect our rights to the same extent as the laws of the United States, or vice versa. There is no assurance that all potentially relevant prior art relating to our patents and patent applications has been found, which can prevent a patent from issuing from a pending application or later invalidate or narrow the scope of an issued patent. For example, publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing or, in some cases, not at all. Therefore, we cannot know with certainty whether we were the first to make the inventions claimed in our patents or pending patent applications, or that we were the first to file for patent protection of such inventions. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending and future patent applications may not result in patents being issued that protect our Wholly Owned Programs or our Founded Entities' therapeutic candidates, in whole or in part, or which effectively prevent others from commercializing competitive therapeutic candidates. Even if our patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. Our competitors may be able to circumvent our patents by developing similar or alternative therapeutic candidates in a non-infringing manner.

In addition, the issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our patents may be challenged in the courts or patent offices in the United States and abroad. Such challenges may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical therapeutic candidates to ours, or limit the duration of the patent protection of our Wholly Owned Programs or our Founded Entities' therapeutic candidates. For example, we may be subject to a third-party preissuance submission of prior art to the USPTO, or become involved in opposition, derivation, reexamination, inter partes review, post-grant review or interference proceedings challenging our owned or licensed patent rights. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our Wholly Owned Programs or our Founded Entities' therapeutic candidates and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize drugs without infringing third-party patent rights. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, regardless of the outcome, it could dissuade companies from collaborating with us to license, develop or commercialize current or future therapeutic candidates.

Furthermore, our and our Founded Entities' intellectual property rights may be subject to a reservation of rights by one or more third parties. We are party to a license agreement with New York University related to certain intellectual property underlying our LYT-200 and LYT-210 therapeutic candidates which is subject to certain rights of the government, including march-in rights, to such intellectual property due to the fact that the research was funded at least in part by the U.S. government. We are also party to other license agreements for intellectual property underlying certain of our therapeutic candidates and programs. Additionally, our Founded Entities Akili, Follica, Vedanta, Sonde, Alivio and Vor, are party to license agreements with academic institutions pursuant to which such Founded Entities have in-licensed certain intellectual property underlying various of their therapeutic candidates. While these license agreements are exclusive, they contain provisions pursuant to which the government has certain rights, including march-in rights, to such patents and technologies due to the fact that the research was funded at least in part by the U.S. government. When new technologies are developed with government funding, the government generally obtains certain rights in any resulting patents, including a non-exclusive license authorizing the government to use the invention or to have others use the invention on its behalf. These rights may permit the government to disclose our information to third parties and to exercise march-in rights to use or allow third parties to use our technology. The government can exercise its march-in rights if it determines that action is necessary because we fail to achieve practical application of the government-funded technology, because action is necessary to alleviate health or safety needs, to meet requirements of federal regulations, or to give preference to U.S. industry. In addition, our rights in such inventions may be subject to certain requirements to manufacture therapeutics embodying such inventions in the United States. Any exercise by the government of such rights or by any third party of its reserved rights could harm our competitive position, business, financial condition, results of operations, and prospects.

If our or our Founded Entities' trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected.

Our or our Founded Entities' registered or unregistered trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. We and our Founded Entities may not be able to protect our rights to these trademarks and trade names, which we need to build name recognition among potential collaborators or customers in our markets of interest. At times, competitors may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of other trademarks or trademarks that incorporate variations of our registered or unregistered trademarks or trade names. Over the long term, if we and our Founded Entities are unable to establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively and our business may be adversely affected. We and our Founded Entities may license our trademarks and trade names to third parties, such as distributors. Though these license agreements may provide guidelines for how our or our Founded Entities' trademarks and trade names may be used, a breach of these agreements or misuse of our trademarks and tradenames by our licensees may jeopardize our rights in or diminish the goodwill associated with our trademarks and trade names. Our or our Founded Entities' efforts to enforce or protect our proprietary rights related to trademarks, trade names, trade secrets, domain names, copyrights or other intellectual property may be ineffective and could result in substantial costs and diversion of resources and could adversely affect our competitive position, business, financial condition, results of operations and prospects.

We may not be able to protect our intellectual property rights throughout the world.

Filing, prosecuting and defending patents on the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In addition, the laws of some foreign countries do not protect or enforce intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we and our Founded Entities may not be able to prevent third parties from practicing our inventions in all countries

outside the United States, or from selling or importing therapeutics made using our inventions in and into the United States or other jurisdictions. Competitors may use our and our Founded Entities' technologies in jurisdictions where we have not obtained patent protection to develop their own therapeutics and may also export infringing therapeutics to territories where we have patent protection, but enforcement is not as strong as that in the United States. These therapeutics may compete with our or our Founded Entities' therapeutics and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets, and other intellectual property protection, particularly those relating to biotechnology and pharmaceutical therapeutics, which could make it difficult for us to stop the infringement of our or our Founded Entities' patents or marketing of competing therapeutics in violation of our proprietary rights generally. Proceedings to enforce our or our Founded Entities' patent rights in foreign jurisdictions, whether or not successful, could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our or our Founded Entities' patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing, and could provoke third parties to assert claims against us or our Founded Entities. We may not prevail in any lawsuits that we or our Founded Entities initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

In some jurisdictions including European Union countries, compulsory licensing laws compel patent owners to grant licenses to third parties. In addition, some countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If we, our Founded Entities or any of our licensors are forced to grant a license to third parties under patents relevant to our or our Founded Entities' business, or if we, our Founded Entities or our licensors are prevented from enforcing patent rights against third parties, our competitive position may be substantially impaired in such jurisdictions.

Our or our Founded Entities' proprietary rights may not adequately protect our technologies and therapeutic candidates, and do not necessarily address all potential threats to our competitive advantage.

The degree of future protection afforded by our or our Founded Entities' intellectual property rights is uncertain because intellectual property rights have limitations, and may not adequately protect our or our Founded Entities' business, or permit us to maintain our competitive advantage. The following examples are illustrative:

- others may be able to make therapeutics that are the same as or similar to the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates but that are not covered by the claims of the patents that we or our Founded Entities own or have exclusively licensed;
- others, including inventors or developers of our or our Founded Entities' owned or in-licensed patented technologies who may become involved with competitors, may independently develop similar technologies that function as alternatives or replacements for any of our or our Founded Entities' technologies without infringing our intellectual property rights;
- we, our Founded Entities or our licensors or our other collaboration partners might not have been the first to conceive and reduce to practice the inventions covered by the patents or patent applications that we or our Founded Entities own or license or will own or license;
- we, our Founded Entities or our licensors or our other collaboration partners might not have been the first to file patent applications covering certain of the patents or patent applications that we or they own or have obtained a license, or will own or will have obtained a license;
- we, our Founded Entities or our licensors may fail to meet obligations to the U.S. government with respect to in-licensed patents and patent applications funded by U.S. government grants, leading to the loss of patent rights;
- it is possible that our or our Founded Entities' pending patent applications will not result in issued patents;
- it is possible that there are prior public disclosures that could invalidate our, our Founded Entities' or our licensors' patents;
- issued patents that we or our Founded Entities own or exclusively license may not provide us with any competitive advantage, or may be held invalid or unenforceable, as a result of legal challenges by our competitors;
- our or our Founded Entities' competitors might conduct R&D activities in countries where we do not have patent rights, or in countries where R&D safe harbor laws exist, and then use the information learned from such activities to develop competitive therapeutics for sale in our major commercial markets;
- ownership, validity or enforceability of our, our Founded Entities' or our licensors' patents or patent applications may be challenged by third parties; and
- the patents of third parties or pending or future applications of third parties, if issued, may have an adverse effect on our business.

Risks Related to Our License Arrangements

The failure to maintain our licenses and realize their benefits may harm our business.

We have acquired and in-licensed certain of our technologies from third parties. We may in the future acquire, in-license or invest in additional technology that we believe would be beneficial to our business. We are subject to a number of risks associated with our acquisition, in-license or investment in technology, including the following:

- diversion of financial and managerial resources from existing operations;
- successfully negotiating a proposed acquisition, in-license or investment in a timely manner and at a price or on terms and conditions favorable to us;
- successfully combining and integrating a potential acquisition into our existing business to fully realize the benefits of such acquisition;
- the impact of regulatory reviews on a proposed acquisition, in-license or investment; and
- the outcome of any legal proceedings that may be instituted with respect to the proposed acquisition, in-license or investment.

If we fail to properly evaluate potential acquisitions, in-licenses, investments or other transactions associated with the creation of new R&D programs or the maintenance of existing ones, we might not achieve the anticipated benefits of any such transaction, we might incur costs in excess of what we anticipate, and management resources and attention might be diverted from other necessary or valuable activities.

Our or our Founded Entities' rights to develop and commercialize our Wholly Owned Programs or our Founded Entities' therapeutic candidates are subject in part to the terms and conditions of licenses granted to us and our Founded Entities by others, and the patent protection, prosecution and enforcement for some of our Wholly Owned Programs or our Founded Entities' therapeutic candidates may be dependent on our and our Founded Entities' licensors.

We and our Founded Entities currently are reliant upon licenses of certain intellectual property rights and proprietary technologies from third parties that are important or necessary to the development of our and our Founded Entities' proprietary technologies, including technologies related to our Wholly Owned Programs and our Founded Entities' therapeutic candidates. These licenses, and other licenses we and they may enter into in the future, may not provide adequate rights to use such intellectual property and proprietary technologies in all relevant fields of use or in all territories in which we or our Founded Entities may wish to develop or commercialize technology and therapeutic candidates in the future. Licenses to additional third-party proprietary technology or intellectual property rights that may be required for our or our Founded Entities' development programs may not be available in the future or may not be available on commercially reasonable terms. In that event, we or our Founded Entities may be required to expend significant time and resources to redesign our proprietary technology or therapeutic candidates or to develop or license replacement technology, which may not be feasible on a technical or commercial basis. If we and our Founded Entities are unable to do so, we may not be able to develop and commercialize technology and therapeutic candidates in fields of use and territories for which we are not granted rights pursuant to such licenses, which could harm our competitive position, business, financial condition, results of operations and prospects significantly.

In some circumstances, we and our Founded Entities may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain and enforce the patents, covering technology that we or our Founded Entities license from third parties. In addition, some of our or our Founded Entities' agreements with our licensors require us to obtain consent from the licensor before we can enforce patent rights, and our licensor may withhold such consent or may not provide it on a timely basis. Therefore, we cannot be certain that our licensors or collaborators will prosecute, maintain, enforce and defend

such intellectual property rights in a manner consistent with the best interests of our business, including by taking reasonable measures to protect the confidentiality of know-how and trade secrets, or by paying all applicable prosecution and maintenance fees related to intellectual property registrations for any of our Wholly Owned Programs or our Founded Entities' therapeutic candidates and proprietary technologies. We and our Founded Entities also cannot be certain that our licensors have drafted or prosecuted the patents and patent applications licensed to us in compliance with applicable laws and regulations, which may affect the validity and enforceability of such patents or any patents that may issue from such applications. This could cause us to lose rights in any applicable intellectual property that we in-license, and as a result our ability to develop and commercialize therapeutic candidates may be adversely affected and we may be unable to prevent competitors from making, using and selling competing therapeutics.

In addition, our or our Founded Entities' licensors may own or control intellectual property that has not been licensed to us and, as a result, we may be subject to claims, regardless of their merit, that we are infringing or otherwise violating the licensor's rights. In addition, while we cannot currently determine the amount of the royalty obligations we would be required to pay on sales of future therapeutics, if any, the amounts may be significant. The amount of our and our Founded Entities' future royalty obligations will depend on the technology and intellectual property we and our Founded Entities use in therapeutic candidates that we successfully develop and commercialize, if any. Therefore, even if we or our Founded Entities successfully develop and commercialize therapeutic candidates, we may be unable to achieve or maintain profitability. In addition, we or our Founded Entities may seek to obtain additional licenses from our licensors and, in connection with obtaining such licenses, we may agree to amend our existing licenses in a manner that may be more favorable to the licensors, including by agreeing to terms that could enable third parties (potentially including our competitors) to receive licenses to a portion of the intellectual property rights that are subject to our or our Founded Entities' existing licenses. Any of these events could have a material adverse effect on our or our Founded Entities' competitive position, business, financial conditions, results of operations, and prospects.

If we or our Founded Entities fail to comply with our obligations in the agreements under which we license intellectual property rights from third parties or these agreements are terminated or we or our Founded Entities otherwise experience disruptions to our business relationships with our licensors, we could lose intellectual property rights that are important to our business.

We are party to various agreements that we depend on to develop our Wholly Owned Programs or our Founded Entities' therapeutic candidates and various proprietary technologies, and our rights to use currently licensed intellectual property, or intellectual property to be licensed in the future, are or will be subject to the continuation of and our and our Founded Entities' compliance with the terms of these agreements. For example, under certain of our and our Founded Entities' license agreements we and our Founded Entities are required to use commercially reasonable efforts to develop and commercialize therapeutic candidates covered by the licensed intellectual property rights, maintain the licensed intellectual property rights, and achieve certain development milestones, each of which could result in termination in the event we or our Founded Entities fail to comply.

In spite of our efforts, our or our Founded Entities' licensors might conclude that we have materially breached our obligations under such license agreements and might therefore terminate the license agreements, thereby removing or limiting our or our Founded Entities' ability to develop and commercialize therapeutics and technology covered by these license agreements.

Moreover, disputes may arise regarding intellectual property subject to a licensing agreement, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- the extent to which our Wholly Owned Programs or our Founded Entities' therapeutic candidates, technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- the sublicensing of patent and other rights under our or our Founded Entities' collaborative development relationships;
- our and our Founded Entities' diligence obligations under the license agreement and what activities satisfy those diligence obligations;
- the inventorship and ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our and our Founded Entities' licensors and us and our Founded Entities and our partners; and
- the priority of invention of patented technology.

In addition, certain provisions in our and our Founded Entities' license agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology, or increase what we believe to be our financial or other obligations under the agreement, either of which could have a material adverse effect on our or our Founded Entities' business, financial condition, results of operations and prospects. Moreover, if disputes over intellectual property that we or our Founded Entities have licensed prevent or impair our ability to maintain our current licensing arrangements on commercially acceptable terms, we may be unable to successfully develop and commercialize the affected therapeutic candidates, which could have a material adverse effect on our competitive position, business, financial conditions, results of operations and prospects.

Third-party claims of intellectual property infringement may prevent or delay our development and commercialization efforts.

Our commercial success depends in part on our avoiding infringement of the patents and proprietary rights of third parties. However, our research, development and commercialization activities may be subject to claims that we infringe or otherwise violate patents or other intellectual property rights owned or controlled by third parties. There is a substantial amount of litigation, both within and outside the United States, involving patent and other intellectual property rights in the biotechnology and pharmaceutical industries, including patent infringement lawsuits, interferences, derivation, oppositions, inter partes review and post-grant review before the USPTO, and corresponding foreign patent offices. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are pursuing development candidates. Our competitors in both the United States and abroad, many of which have substantially greater resources and have made substantial investments in patent portfolios and competing technologies, may have applied for or obtained or may in the future apply for or obtain, patents that will prevent, limit or otherwise interfere with our ability to make, use and sell, if approved, the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates. In addition, many companies in the biotechnology and pharmaceutical industries have employed intellectual property litigation as a means to gain an advantage over their competitors. As the biotechnology and pharmaceutical industries expand and more patents are issued, and as we gain greater visibility and market exposure as a public company, the risk increases that our existing therapeutic candidates and any other therapeutic candidates that we or our Founded Entities may identify may be subject to claims of infringement of the patent rights of third parties.

There may be other third-party patents or patent applications with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our or our Founded Entities' existing therapeutic candidates and any other therapeutic candidates that we or they may identify. Because patent applications can take many years to issue, there may be currently pending patent applications which may later result in issued patents that our or our Founded Entities' existing therapeutic candidates and any other therapeutic candidates that we or they may identify may infringe. In addition, third parties may obtain patents in the future and claim that use of our or our Founded Entities' technologies infringes upon these patents. If any third-party patents were held by a court of competent jurisdiction to cover the manufacturing process of our or our Founded Entities' existing therapeutic candidates and any other therapeutic candidates that we or they may identify, any molecules formed during the manufacturing process, or any final therapeutic itself, the holders of any such patents may be able to block our ability to commercialize such therapeutic candidate unless we obtained a license under the applicable patents, or until such patents expire. Additionally, pending patent applications that have been published can, subject to certain limitations, be later amended in a manner that could cover our Wholly Owned Programs or our Founded Entities' therapeutic candidates. Furthermore, the scope of a patent claim is determined by an interpretation of the law, the written disclosure in a patent and the patent's prosecution history and can involve other factors such as expert opinion. Our analysis of these issues, including interpreting the relevance or the scope of claims in a patent or a pending application, determining applicability of such claims to our proprietary technologies or therapeutic candidates, predicting whether a third party's pending patent application will issue with claims of relevant scope, and determining the expiration date of any patent in the United States or abroad that we consider relevant may be incorrect, which may negatively impact our or our Founded Entities' ability to develop and market the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates. We do not always conduct independent reviews of pending patent applications of and patents issued to third parties.

Similarly, if any third-party patents were held by a court of competent jurisdiction to cover aspects of our or our Founded Entities' formulations, processes for manufacture or methods of use, including any combination therapies, the holders of any such patents may be able to block our or

our Founded Entities' ability to develop and commercialize the applicable therapeutic candidate unless we obtained a license or until such patent expires. In either case, such a license may not be available on commercially reasonable terms or at all, or it may be non-exclusive, which could result in our competitors gaining access to the same intellectual property.

Parties making claims against us or our Founded Entities may obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize our or our Founded Entities' existing therapeutic candidates and any other therapeutic candidates that we may identify. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of management and employee resources from our business. In the event of a successful claim of infringement against us or our Founded Entities, we or our Founded Entities may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, pay royalties, redesign our infringing therapeutics or obtain one or more licenses from third parties, which may be impossible or require substantial time and monetary expenditure.

Parties making claims against us or our Founded Entities may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation or administrative proceedings, there is a risk that some of our confidential information could be compromised by disclosure. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have material adverse effect on our ability to raise additional funds or otherwise have a material adverse effect on our business, results of operations, financial condition and prospects.

Risks Related to Our Patents

Patent terms may be inadequate to protect our competitive position on therapeutic candidates for an adequate amount of time.

Patents have a limited lifespan. In the United States, if all maintenance fees are timely paid, the natural expiration of a patent is generally 20 years from its earliest U.S. non-provisional or international patent application filing date. Various extensions may be available, but the life of a patent, and the protection it affords, is limited. Even if patents covering our Wholly Owned Programs or our Founded Entities' therapeutic candidates are obtained, once the patent life has expired, we or our Founded Entities may be open to competition from competitive therapeutics, including generics or biosimilars. Given the amount of time required for the development, testing and regulatory review of new therapeutic candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our or our Founded Entities' owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing therapeutics similar or identical to ours.

If we or our Founded Entities are not able to obtain patent term extension or non-patent exclusivity in the United States under the Hatch-Waxman Act and in foreign countries under similar legislation, thereby potentially extending the marketing exclusivity term of the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates, our business may be materially harmed.

Depending upon the timing, duration and specifics of FDA marketing approval of the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates, one or more of the U.S. patents covering each of such therapeutic candidates or the use thereof may be eligible for up to five years of patent term extension under the Hatch-Waxman Act. The Hatch-Waxman Act allows a maximum of one patent to be extended per new drug application, or NDA, for an FDA approved therapeutic as compensation for the patent term lost during the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of therapeutic approval and only those claims covering such approved drug therapeutic, a method for using it or a method for manufacturing it may be extended. Patent term extension also may be available in certain foreign countries upon regulatory approval of the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates. Nevertheless, we or our Founded Entities may not be granted patent term extension either in the United States or in any foreign country because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. Moreover, the term of extension, as well as the scope of patent protection during any such extension, afforded by the governmental authority could be less than we request.

If we or our Founded Entities are unable to obtain patent term extension or restoration, or the term of any such extension is less than our request, the period during which we will have the right to exclusively market our therapeutic may be shortened and our competitors may obtain approval of competing therapeutics following our patent expiration sooner, and our revenue could be reduced, possibly materially.

Further, for certain of our and our Founded Entities' licensed patents, we and our Founded Entities do not have the right to control prosecution, including filing with the USPTO, a petition for patent term extension under the Hatch-Waxman Act. Thus, if one of our or our Founded Entities' licensed patents is eligible for patent term extension under the Hatch-Waxman Act, we may not be able to control whether a petition to obtain a patent term extension is filed with, or whether a patent term extension is obtained from, the USPTO.

Also, there are detailed rules and requirements regarding the patents that may be submitted to the FDA for listing in the Approved Drug Products with Therapeutic Equivalence Evaluations, or the Orange Book. We or our Founded Entities may be unable to obtain patents covering the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates that contain one or more claims that satisfy the requirements for listing in the Orange Book. Even if we or our Founded Entities submit a patent for listing in the Orange Book, the FDA may decline to list the patent, or a manufacturer of generic drugs may challenge the listing. If or when one of the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates is approved and a patent covering that therapeutic candidate is not listed in the Orange Book, a manufacturer of generic drugs would not have to provide advance notice to us of any abbreviated new drug application, or ANDA, filed with the FDA to obtain permission to sell a generic version of such therapeutic candidate.

Issued patents covering our Wholly Owned Programs or our Founded Entities' therapeutic candidates could be found invalid or unenforceable if challenged in courts or patent offices.

If we, our Founded Entities or one of our licensing partners initiated legal proceedings against a third party to enforce a patent covering one or more of our Wholly Owned Programs or our Founded Entities' therapeutic candidates, the defendant could counterclaim that the patent covering the relevant therapeutic candidate is invalid and/or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including subject matter eligibility, novelty, nonobviousness, written description or enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during prosecution. Third parties may also raise similar claims before administrative bodies in the United States or abroad, even outside the context of litigation. Such mechanisms include re-examination, post grant review, and equivalent proceedings in foreign jurisdictions (e.g., opposition proceedings). Such proceedings could result in revocation or amendment to our or our Founded Entities' patents in such a way that they no longer cover our Wholly Owned Programs or our Founded Entities' therapeutic candidates. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which we and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, we would lose at least part, and perhaps all, of the patent protection on our Wholly Owned Programs or our Founded Entities' therapeutic candidates. Such a loss of patent protection could have a material adverse impact on our business.

Changes in U.S. patent law could diminish the value of patents in general, thereby impairing our and our Founded Entities' ability to protect our therapeutics.

Changes in either the patent laws or interpretation of the patent laws in the United States could increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents. Assuming that other requirements for patentability are met, prior to March 2013, in the United States, the first to invent the claimed invention was entitled to a patent, while outside the United States, the first to file a patent application was entitled to the patent. After March 2013, under the Leahy-Smith America Invents Act, or the America Invents Act, enacted in September 2011, the United States transitioned to a first inventor to file system in which, assuming that other requirements for patentability are met, the first inventor to file a patent application will be entitled to the patent on an invention regardless of whether a third party was the first to invent the claimed invention. A third party that files a patent application in the USPTO after March 2013, but before us could therefore be awarded a patent covering an invention of ours even if we had made the invention before it was made by such third party. This will require us and our Founded Entities to be cognizant of the time from invention to filing of a patent application and be diligent in filing patent applications, but circumstances could prevent us from promptly filing patent applications on our inventions. Since patent applications in the United States and most other countries are confidential for a period of time after filing or until issuance, we cannot be certain that we, our Founded Entities or our licensors were the first to either (i) file any patent application related to our

Wholly Owned Programs or our Founded Entities' therapeutic candidates or (ii) invent any of the inventions claimed in our, our Founded Entities or our licensor's patents or patent applications.

The America Invents Act also includes a number of significant changes that affect the way patent applications are prosecuted and also may affect patent litigation. These include allowing third party submission of prior art to the USPTO during patent prosecution and additional procedures to attack the validity of a patent by USPTO administered post-grant proceedings, including post-grant review, inter partes review, and derivation proceedings. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in U.S. federal courts necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action. Accordingly, a third party may attempt to use the USPTO procedures to invalidate our patent claims that would not have been invalidated if first challenged by the third party as a defendant in a district court action. Therefore, the America Invents Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our or our Founded Entities' owned or in-licensed patent applications and the enforcement or defense of our or our Founded Entities' owned or in-licensed issued patents, all of which could have a material adverse effect on our competitive position, business, financial condition, results of operations, and prospects.

In addition, the patent positions of companies in the development and commercialization of pharmaceuticals are particularly uncertain. Recent U.S. Supreme Court and Federal Circuit rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. This combination of events has created uncertainty with respect to the validity and enforceability of patents, once obtained. Depending on future actions by the U.S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that could have a material adverse effect on our existing patent portfolio and our ability to protect and enforce our intellectual property in the future.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and/or applications will be due to be paid to the USPTO and various governmental patent agencies outside of the United States in several stages over the lifetime of the patents and/or applications. We and our Founded Entities have systems in place to remind us to pay these fees, and we and our Founded Entities employ outside firms and rely on outside counsel to pay these fees due to the USPTO and non-U.S. patent agencies. However, we and our Founded Entities cannot guarantee that our licensors have similar systems and procedures in place to pay such fees. In addition, the USPTO and various non-U.S. governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. We employ reputable law firms and other professionals to help us comply, and in many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. However, there are situations in which non-compliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, our competitors might be able to enter the market and this circumstance would have a material adverse effect on our business.

Risks Related to Confidentiality

If we are unable to protect the confidentiality of our trade secrets, the value of our technology could be materially adversely affected and our business would be harmed.

We and our Founded Entities consider proprietary trade secrets, confidential know-how and unpatented know-how to be important to our business. We and our Founded Entities may rely on trade secrets and confidential know-how to protect our technology, especially where patent protection is believed by us to be of limited value. However, trade secrets and confidential know-how are difficult to protect, and we have limited control over the protection of trade secrets and confidential know-how used by our licensors, collaborators and suppliers. Because we have relied in the past on third parties to manufacture the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates, because we may continue to do so in the future, and because we expect to collaborate with third parties on the development of our current therapeutic candidates and any future therapeutic candidates we develop, we may, at times, share trade secrets with them. We also conduct joint R&D programs that may require us to share trade secrets under the terms of our R&D partnerships or similar agreements. Under such circumstances, trade secrets and confidential know-how can be difficult to maintain as confidential.

We and our Founded Entities seek to protect our confidential proprietary information, in part, by confidentiality agreements and invention assignment agreements with our employees, consultants, scientific advisors, contractors and collaborators. These agreements are designed to protect our proprietary information. However, we cannot be certain that such agreements have been entered into with all relevant parties, and we cannot be certain that our and our Founded Entities' trade secrets and other confidential proprietary information will not be disclosed or that competitors will not otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques. For example, any of these parties may breach the agreements and disclose proprietary information, including trade secrets, and we may not be able to obtain adequate remedies for such breaches. We and our Founded Entities also seek to preserve the integrity and confidentiality of our confidential proprietary information by maintaining physical security of our premises and physical and electronic security of our information technology systems, but it is possible that these security measures could be breached. If any of our or our Founded Entities' confidential proprietary information were to be lawfully obtained or independently developed by a competitor, we or our Founded Entities would have no right to prevent such competitor from using that technology or information to compete with us, which could harm our competitive position.

Unauthorized parties may also attempt to copy or reverse engineer certain aspects of our or our Founded Entities' therapeutics that we consider proprietary. We or our Founded Entities may not be able to obtain adequate remedies in the event of such unauthorized use. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret can be difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets. Trade secrets will also over time be disseminated within the industry through independent development, the publication of journal articles and the movement of personnel skilled in the art from company to company or academic to industry scientific positions. Though our or our Founded Entities' agreements with third parties typically restrict the ability of our advisors, employees, collaborators, licensors, suppliers, third-party contractors and consultants to publish data potentially relating to our trade secrets, our agreements may contain certain limited publication rights. In addition, if any of our or our Founded Entities' trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent such competitor from using that technology or information to compete with us, which could harm our competitive position. Despite employing the contractual and other security precautions described above, the need to share trade secrets increases the risk that such trade secrets become known by our competitors, are inadvertently incorporated into the technology of others, or are disclosed or used in violation of these agreements. If any of these events occurs or if we otherwise lose protection for our trade secrets, the value of such information may be greatly reduced and our competitive position, business, financial condition, results of operations, and prospects would be harmed.

We or our Founded Entities may be subject to claims that our employees, consultants or independent contractors have wrongfully used or disclosed confidential information of third parties or that our employees have wrongfully used or disclosed alleged trade secrets of their former employers.

As is common in the biotechnology and pharmaceutical industries, we and our Founded Entities employ individuals who were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we and our Founded Entities try to ensure that our employees, consultants and independent contractors do not use the proprietary information or know-how of others in their work for us, we or our Founded Entities may be subject to claims that we or our employees, consultants or independent contractors have inadvertently or otherwise used or disclosed intellectual property, including trade secrets or other proprietary information, of any of our employee's former employer or other third parties. Litigation may be necessary to defend against these claims. If we or our Founded Entities fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel, which could adversely impact our business. Even if we or our Founded Entities are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

Risks Related to Challenges or Lawsuits Related to Intellectual Property

We may become involved in lawsuits to protect or enforce our or our Founded Entities' patents or other intellectual property, which could be expensive, time consuming and unsuccessful.

Competitors may infringe our or our Founded Entities' patents or other intellectual property. Our and our Founded Entities' ability to enforce our

patent or other intellectual property rights depends on our ability to detect infringement. It may be difficult to detect infringers who do not advertise the components or methods that are used in connection with their therapeutics and services. Moreover, it may be difficult or impossible to obtain evidence of infringement in a competitor's or potential competitor's therapeutic or service. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded if we were to prevail may not be commercially meaningful. If we were to initiate legal proceedings against a third party to enforce a patent covering one or more of our Wholly Owned Programs or our Founded Entities' therapeutic candidates, the defendant could counterclaim that the patent covering our or our Founded Entities' therapeutic candidate is invalid and/or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including subject matter eligibility, novelty, nonobviousness, written description or enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during prosecution. The outcome following legal assertions of invalidity and unenforceability is unpredictable. Interference or derivation proceedings provoked by third parties or brought by us or declared by the USPTO may be necessary to determine the priority of inventions with respect to our or our Founded Entities' patents or patent applications. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms or at all, or if a non-exclusive license is offered and our competitors gain access to the same technology. Our defense of litigation or interference or derivation proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees. In addition, the uncertainties associated with litigation could have a material adverse effect on our ability to raise the funds necessary to continue clinical trials, continue research programs, license necessary technology from third parties, or enter into development partnerships that would help us bring therapeutic candidates to market. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our or our Founded Entities' confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions, or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could adversely impact the price of our ADSs. Furthermore, any of the foregoing could have a material adverse effect on our financial condition, results of operations, and prospects.

We and our Founded Entities may be subject to claims challenging the inventorship of our patents and other intellectual property.

Our and our Founded Entities' agreements with employees and our personnel policies provide that any inventions conceived by an individual in the course of rendering services to us shall be our exclusive property. Although our policy is to have all such individuals complete these agreements, we may not obtain these agreements in all circumstances, and individuals with whom we have these agreements may not comply with their terms. The assignment of intellectual property may not be automatic upon the creation of an invention and despite such agreement, such inventions may become assigned to third parties. In the event of unauthorized use or disclosure of our trade secrets or proprietary information, these agreements, even if obtained, may not provide meaningful protection, particularly for our trade secrets or other confidential information.

We, our Founded Entities or our licensors may be subject to claims that former employees, collaborators or other third parties have an interest in our owned or in-licensed patents, trade secrets, or other intellectual property as an inventor or co-inventor. For example, we, our Founded Entities or our licensors may have inventorship disputes arising from conflicting obligations of employees, consultants or others who are involved in developing our Wholly Owned Programs or our Founded Entities' therapeutic candidates. Litigation may be necessary to defend against these and other claims challenging inventorship of our, our Founded Entities' or our licensors' ownership of our owned or in-licensed patents, trade secrets or other intellectual property. If we, our Founded Entities or our licensors fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, intellectual property that is important to our Wholly Owned Programs or our Founded Entities' therapeutic candidates. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

Any of the foregoing could have a material adverse effect on our competitive position, business, financial condition, results of operations and prospects.

Risks Related to the COVID-19 Pandemic

The COVID- 19 pandemic has impacted, and will likely continue to impact, our business, including our clinical trials and preclinical studies, and may materially and adversely affect our business in the future.

Public health crises such as pandemics or other global emergencies could adversely impact our business. In response to the spread of COVID-19 and governmental shelter-in-place orders, we encouraged our administrative employees to work outside of our offices and allowed staff in our laboratory facilities to operate under applicable government orders and protocols designed to protect their health and safety. Many of these restrictions have since been eased or lifted in a phased-in approach over time. However, these government policies and directives are subject to change, including that additional, more restrictive orders, proclamations and/or directives may be issued in the future, as the effects and spread of the COVID-19 pandemic continue to evolve.

As a result of the COVID-19 outbreak or any future pandemics, we have experienced, and may in the future experience, disruptions that severely impact our business, clinical trials and preclinical studies, including:

- delays or difficulties in enrolling patients in our clinical trials;
- delays or difficulties in clinical site initiation, including difficulties in recruiting clinical site investigators and clinical site staff;
- delays or disruptions in non-clinical experiments due to unforeseen circumstances at contract research organizations, or CROs, and vendors along their supply chain;
- increased rates of patients withdrawing from our clinical trials following enrollment as a result of contracting COVID-19, being forced to quarantine, or not accepting home health visits;
- diversion of healthcare resources away from the conduct of clinical trials, including the diversion of hospitals serving as our clinical trial sites and hospital staff supporting the conduct of our clinical trials;
- interruption of key clinical trial activities, such as clinical trial site data monitoring, due to limitations on travel imposed or recommended by federal or state governments, employers and others or interruption of clinical trial subject visits and study procedures (particularly any procedures that may be deemed non-essential), which may impact the integrity of subject data and clinical study endpoints;
- interruption or delays in the operations of the FDA and comparable foreign regulatory agencies, which may impact review and approval timelines;
- interruption of, or delays in receiving, supplies of our therapeutic candidates from our contract manufacturing organizations due to staffing shortages, production slowdowns or stoppages and disruptions in delivery systems; and
- limitations on employee resources that would otherwise be focused on the conduct of our preclinical studies and clinical trials, including because of sickness of employees or their families, the desire of employees to avoid contact with large groups of people, an increased reliance on working from home or mass transit disruptions.

These and other factors arising from the COVID-19 pandemic could worsen in countries that are already afflicted with COVID-19, could continue to spread to additional countries, or could return to countries where the pandemic has been partially contained, each of which could further adversely impact our ability to conduct clinical trials and our business generally, and could have a material adverse impact on our operations and financial condition and results.

In addition, the trading prices for biopharmaceutical companies have been highly volatile as a result of the COVID-19 pandemic. As a result, if we require any further capital we may face difficulties raising capital through sales of our common stock or such sales may be on unfavorable terms. The COVID-19 outbreak continues to rapidly evolve. The extent to which the outbreak may impact our business, preclinical studies and clinical trials will depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the ultimate geographic spread of the disease, the duration of the outbreak, travel restrictions and actions to contain the outbreak or treat its impact, such as social distancing and quarantines or lock-downs in the United States and other countries, business closures or business disruptions and the effectiveness of actions taken in the United States and other countries to contain and treat the disease.

To the extent the COVID-19 pandemic adversely affects our business and financial results, it may also have the effect of heightening many of the other risks described in this "Risk Factors" section, such as those relating to our clinical development operations, the supply chain for our ongoing and planned clinical trials, and the availability of governmental and regulatory authorities to conduct inspections of our clinical trial sites, review materials submitted by us in support of our applications for regulatory approval and grant approval for our therapeutic candidates.

We may not be successful in our efforts to develop LYT-100 for the treatment of Long COVID respiratory complications and related sequelae.

We have initiated and fully enrolled a global, randomized, double-blind, placebo-controlled Phase 2 trial designed to evaluate the efficacy, safety and tolerability of LYT-100 in adults with post-acute COVID-19 respiratory complications. The primary endpoint is a standardized test of how far a patient can walk in six minutes. Secondary endpoints, including pharmacokinetics, inflammatory biomarkers, imaging, and patient-reported outcomes will also be evaluated.

Given the rapidity of the onset of the COVID-19 pandemic, scientific and medical research on the SARS-CoV-2 virus is ongoing and evolving. We cannot be certain that the evidence that we believe suggests that LYT-100 may be beneficial to these patients will be established in a clinical trial. The failure of LYT-100 to demonstrate safety and efficacy in these patients could negatively impact the perception of us and LYT-100 by investors and it is possible that unexpected safety issues could occur in these COVID-19 patients. Any such safety issues could affect our development plans for LYT-100 in other indications.

Risks Related to Our Business and Industry

We attempt to distribute our scientific, execution and financing risks across a variety of therapeutic areas, indications, programs and modalities that relate to the brain, immune system and gastrointestinal system and the interface between them. However, our assessment of, and approach to, risk may not be comprehensive or effectively avoid delays or failures in one or more of our programs. Failures in one or more of our programs could adversely impact other programs and have a material adverse impact on our business, results of operations and ability to fund our business.

We are dedicated to discovering, developing and commercializing highly differentiated medicines for devastating diseases, including inflammatory, fibrotic and immunological conditions, intractable cancers, lymphatic and gastrointestinal diseases and neurological and neuropsychological disorders, among others. Across the entire portfolio, we established the underlying programs and platforms that have resulted in 27 therapeutics and therapeutic candidates that are being advanced within our Wholly Owned Programs or by our Founded Entities. Of these therapeutics and therapeutic candidates, 16 are clinical-stage and two have been cleared for marketing by the FDA and granted marketing authorization in the EEA and in other countries that recognize the CE Mark. Our publicly-listed Founded Entities, Karuna, Vor and Gelesis, are advancing seven of these therapeutic candidates, including two that are currently in Phase 3/Pivotal studies, as well as one FDA-authorized therapeutic. Our privately-held Founded Entities, Akili, Vedanta, Follica, Sonde and Entrega, are advancing 13 other therapeutic candidates, including two that are expected to enter a pivotal study. Finally, we are advancing seven therapeutic candidates within our Wholly Owned Pipeline, including one therapeutic candidate that is being advanced in collaboration with a pharmaceutical company, with two Phase 2 and two Phase 1 clinical trials underway. We and our Founded Entities have relationships with several pharmaceutical companies or their investment arms to advance some of the programs and platforms underlying these therapeutics and therapeutic candidates. As our and certain of our Founded Entities' therapeutic candidates progress through clinical development, we or others may determine that certain of our risk allocation decisions were incorrect or insufficient, that individual programs or our science in general has technology or biology risks that were unknown or underappreciated, or that we have allocated resources across our programs in such a way that did not maximize potential value creation. All of these risks may relate to our current and future programs sharing similar science and infrastructure, and in the event material decisions in any of these areas turn out to have been incorrect or under-optimized, we may experience a material adverse impact on our business and ability to fund our operations.

Our business is highly dependent on the clinical advancement of our programs and our success in identifying potential therapeutic candidates across the brain, immune and gastrointestinal therapeutic areas. Delay or failure to advance our programs could adversely impact our business.

We are developing new medicines based on the lymphatic system and the brain, immune and gastrointestinal therapeutic areas. Over time, our and our Founded Entities' preclinical and clinical work led us to identify potential synergies across target therapeutic indications in the brain, immune and gastrointestinal areas, generating a broad portfolio of therapeutic candidates across multiple programs. Even if a particular program is successful in any phase of development, such program could fail at a later phase of development, and other programs within the same therapeutic area may still fail at any phase of development including at phases where earlier programs in that therapeutic area were successful. This may be a result of technical challenges unique to that program or due to biology risk, which is unique to every program. As we progress our programs through clinical development, there may be new technical challenges that arise that cause an entire program or a group of programs within an area of focus in the brain, immune and gastrointestinal therapeutic areas to fail. While we aim to segregate risk across programs, and in certain cases among our Founded Entities, there may be foreseen and unforeseen risks across the therapeutic candidates within our Wholly Owned Pipeline and programs being developed by our Founded Entities in whole or in part. In addition, if any one or more of our clinical programs encounter safety, tolerability, or efficacy problems, developmental delays, regulatory issues, or other problems, our business could be significantly harmed.

Our future success depends on our ability to retain key employees, directors, consultants and advisors and to attract, retain and motivate qualified personnel.

Our ability to compete in the highly competitive biotechnology industry depends upon our ability to attract and retain highly qualified managerial, scientific and medical personnel. We are highly dependent on the management, R&D, clinical, financial and business development expertise of our executive officers, our directors, as well as the other members of our scientific and clinical teams, including Daphne Zohar, our chief executive officer, Bharatt Chowrira, our president and chief business, legal and operating officer, George Farmer, our chief financial officer, Eric Elenko, our chief innovation and strategy officer, Joseph Bolen, our chief scientific officer, and Julie Krop, our chief medical officer. The loss of the services of any of our executive officers and other key personnel, and our inability to find suitable replacements could result in delays in therapeutic development and our financial condition and results of operations could be materially adversely affected.

Furthermore, each of our executive officers may terminate their employment with us at any time. Recruiting and retaining qualified scientific and clinical personnel and, if we progress the development of the therapeutic candidates within our Wholly Owned Pipeline toward scaling up for commercialization, sales and marketing personnel, will also be critical to our success. The loss of the services of our executive officers or other key employees could impede the achievement of research, development and commercialization objectives and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval for and commercialize the therapeutic candidates within our Wholly Owned Pipeline. Competition to hire qualified personnel in our industry is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. Furthermore, to the extent we hire personnel from competitors, we may be subject to allegations that they have been improperly solicited or that they have divulged proprietary or other confidential information, or that their former employers own their research output. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions.

In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. If we are unable to continue to attract and retain high quality personnel, our ability to pursue our growth strategy will be limited.

We will need to expand our organization and we may experience difficulties in managing this growth, which could disrupt our operations.

As we mature, we expect to expand our full-time employee base and to hire more consultants and contractors. Our management may need to divert a disproportionate amount of its attention away from our day-to-day activities and devote a substantial amount of time toward managing these growth activities. We may not be able to effectively manage the expansion of our operations, which may result in weaknesses in our infrastructure, operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees. Our expected growth could require significant capital expenditures and may divert financial resources from other projects, such as the development of additional therapeutic candidates. If our management is unable to effectively manage our growth, our expenses may increase more than expected, our ability to generate and/or grow revenues could be reduced, and we may not be able to implement our business strategy. Our future financial performance and our ability to commercialize therapeutic candidates and compete effectively will depend, in part, on our ability to effectively manage any future growth.

Because we are developing multiple programs and therapeutic candidates and are pursuing a variety of target indications and treatment modalities, we may expend our limited resources to pursue a particular therapeutic candidate and fail to capitalize on development opportunities or therapeutic candidates that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and personnel resources, we may forgo or delay pursuit of opportunities with potential target indications or therapeutic candidates that later prove to have greater commercial

potential than our current and planned development programs and therapeutic candidates. Our resource allocation decisions may cause us to fail to capitalize on viable commercial therapeutics or profitable market opportunities. Our spending on current and future research and development programs and other future therapeutic candidates for specific indications may not yield any commercially viable future therapeutic candidates. If we do not accurately evaluate the commercial potential or target market for a particular therapeutic candidate, we may be required to relinquish valuable rights to that therapeutic candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such future therapeutic candidates.

Additionally, we may pursue additional in-licenses or acquisitions of development-stage assets or programs, which entails additional risk to us. For example, in 2019 we acquired LYT-100, which is the most advanced therapeutic candidate in our Wholly Owned Pipeline and to which we are investing significant resources for its development. Identifying, selecting and acquiring promising therapeutic candidates requires substantial technical, financial and human resources expertise. Efforts to do so may not result in the actual acquisition or license of a successful therapeutic candidate, potentially resulting in a diversion of our management's time and the expenditure of our resources with no resulting benefit. For example, if we are unable to identify programs that ultimately result in approved therapeutics, we may spend material amounts of our capital and other resources evaluating, acquiring and developing therapeutics that ultimately do not provide a return on our investment.

Product liability lawsuits against us could cause us to incur substantial liabilities and could limit commercialization of any therapeutic candidates that we may develop.

We face an inherent risk of product liability exposure related to the testing of therapeutic candidates in human clinical trials and will face an even greater risk if we commercially sell any therapeutics that we may develop. If we cannot successfully defend ourselves against claims that the therapeutic candidates within our Wholly Owned Pipeline or medicines caused injuries, we could incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for any therapeutic candidates or medicines that we may develop;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- significant costs to defend the related litigation;
- substantial monetary awards to trial participants or patients;
- loss of revenue; and
- the inability to commercialize the therapeutic candidates within our Wholly Owned Pipeline.

Although we maintain product liability insurance, including coverage for clinical trials that we sponsor, it may not be adequate to cover all liabilities that we may incur. We anticipate that we will need to increase our insurance coverage as we commence additional clinical trials and if we successfully commercialize any therapeutic candidates. The market for insurance coverage is increasingly expensive, and the costs of insurance coverage will increase as our clinical programs increase in size. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise.

The increasing use of social media platforms presents new risks and challenges.

Social media is increasingly being used to communicate about our and our Founded Entities' clinical development programs and the diseases our therapeutics are being developed to treat, and we intend to utilize appropriate social media in connection with our commercialization efforts following approval of the therapeutic candidates within our Wholly Owned Pipeline. Social media practices in the biopharmaceutical industry continue to evolve and regulations relating to such use are not always clear. This evolution creates uncertainty and risk of noncompliance with regulations applicable to our business. For example, patients may use social media channels to comment on their experience in an ongoing blinded clinical study or to report an alleged adverse event. When such disclosures occur, there is a risk that we fail to monitor and comply with applicable adverse event reporting obligations or we may not be able to defend our business or the public's legitimate interests in the face of the political and market pressures generated by social media due to restrictions on what we may say about the therapeutic candidates within our Wholly Owned Pipeline. There is also a risk of inappropriate disclosure of sensitive information or negative or inaccurate posts or comments about us on any social networking website. If any of these events were to occur or we otherwise fail to comply with applicable regulations, we could incur liability, face regulatory actions or incur other harm to our business.

Our and our Founded Entities' employees, independent contractors, consultants, commercial partners and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements.

We are exposed to the risk of fraud, misconduct or other illegal activity by our employees, independent contractors, consultants, commercial partners and vendors as well as the employees, independent contractors, consultants, commercial partners and vendors of our Founded Entities. Misconduct by these parties could include intentional, reckless and negligent conduct that fails to: comply with the laws of the FDA and comparable foreign regulatory authorities; provide true, complete and accurate information to the FDA and comparable foreign regulatory authorities; comply with manufacturing standards we have established; comply with healthcare fraud and abuse laws in the United States and similar foreign fraudulent misconduct laws; or report financial information or data accurately or to disclose unauthorized activities. If we or our Founded Entities obtain FDA approval of the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates and begin commercializing those therapeutics in the United States, our potential exposure under such laws will increase significantly, and our costs associated with compliance with such laws are also likely to increase. In particular, research, sales, marketing, education and other business arrangements in the healthcare industry are subject to extensive laws designed to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, educating, marketing and promotion, sales and commission, certain customer incentive programs and other business arrangements generally. Activities subject to these laws also involve the improper use of information obtained in the course of patient recruitment for clinical trials, which could result in regulatory sanctions and cause serious harm to our reputation. It is not always possible to identify and deter misconduct by employees and third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant fines or other sanctions.

Employee litigation and unfavorable publicity could negatively affect our future business.

Our employees may, from time to time, bring lawsuits against us regarding injury, creating a hostile work place, discrimination, wage and hour disputes, sexual harassment, or other employment issues. In recent years, there has been an increase in the number of discrimination and harassment claims generally. Coupled with the expansion of social media platforms and similar devices that allow individuals access to a broad audience, these claims have had a significant negative impact on some businesses. Certain companies that have faced employment- or harassment-related lawsuits have had to terminate management or other key personnel, and have suffered reputational harm that has negatively impacted their business. If we were to face any employment-related claims, our business could be negatively affected.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could harm our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste therapeutics. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties for failure to comply with such laws and regulations.

Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research,

development or therapeutic efforts. Our failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Cyber-attacks or other failures in our telecommunications or information technology systems, or those of our collaborators, contract research organizations, third-party logistics providers, distributors or other contractors or consultants, could result in information theft, data corruption and significant disruption of our business operations.

We, our collaborators, our CROs, third-party logistics providers, distributors and other contractors and consultants utilize information technology, or IT, systems and networks to process, transmit and store electronic information in connection with our business activities. As use of digital technologies has increased, cyber incidents, including third parties gaining access to employee accounts using stolen or inferred credentials, computer malware, viruses, spamming, phishing attacks or other means, and deliberate attacks and attempts to gain unauthorized access to computer systems and networks, have increased in frequency and sophistication. These threats pose a risk to the security of our, our collaborators', our CROs', third-party logistics providers', distributors' and other contractors' and consultants' systems and networks, and the confidentiality, availability and integrity of our data. There can be no assurance that we will be successful in preventing cyber-attacks or successfully mitigating their effects. Similarly, there can be no assurance that our collaborators, CROs, third-party logistics providers, distributors and other contractors and consultants will be successful in protecting our clinical and other data that is stored on their systems. Although to our knowledge we have not experienced any such material system failure or material security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of development programs and business operations.

Any cyber-attack, data breach or destruction or loss of data could result in a violation of applicable U.S. and international privacy, data protection and other laws, and subject us to litigation and governmental investigations and proceedings by federal, state and local regulatory entities in the United States and by international regulatory entities, resulting in exposure to material civil and/or criminal liability. Further, our general liability insurance and corporate risk program may not cover all potential claims to which we are exposed and may not be adequate to indemnify us for all liability that maybe imposed; and could have a material adverse effect on our business and prospects. For example, the loss of clinical trial data from completed or ongoing clinical trials for any of the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates could result in delays in our development and regulatory approval efforts and significantly increase our costs to recover or reproduce the data. In addition, we may suffer reputational harm or face litigation or adverse regulatory action as a result of cyber-attacks or other data security breaches and may incur significant additional expense to implement further data protection measures.

Changes in funding for the FDA, the SEC and other government agencies could hinder their ability to hire and retain key leadership and other personnel, prevent new therapeutics and services from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal functions on which the operation of our business may rely, which could negatively impact our business.

The ability of the FDA to review and approve new therapeutics or take action with respect to other regulatory matters can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept payment of user fees, and statutory, regulatory, and policy changes. In addition, government funding of the SEC and other government agencies on which our operations may rely, including those that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable. The priorities of the FDA may also influence the ability of the FDA to take action on regulatory matters, for example the FDA's budget and funding levels and ability to hire and retain key personnel.

Disruptions at the FDA and other agencies may also slow the time necessary for new drugs to be reviewed and/or approved, or for other actions to be taken, by relevant government agencies, which would adversely affect our business. For example, over the last several years, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA and the SEC, have had to furlough critical FDA, SEC and other government employees and stop critical activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Similarly, a prolonged government shutdown could prevent the timely review of our patent applications by the USPTO, which could delay the issuance of any U.S. patents to which we might otherwise be entitled. Further, in our operations as a public company, future government shutdowns could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

Separately, foreign and domestic inspections by the FDA were largely on hold during the COVID-19 pandemic. Should the FDA determine that an inspection is necessary for approval of a marketing application and an inspection cannot be completed during the review cycle due to restrictions on travel or for other reasons, the FDA has stated that it generally intends to issue a complete response letter. Further, if there is inadequate information to make a determination on the acceptability of a facility, the FDA may defer action on the application until an inspection can be completed. For example, in 2020, several companies announced receipt of complete response letters due to the FDA's inability to complete required inspections for their applications. Regulatory authorities outside the U.S. may adopt similar restrictions or other policy measures in response to the COVID-19 pandemic or for other reasons and may experience delays in their regulatory activities. If a prolonged government shutdown or other disruption occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Future shutdowns or other disruptions could also affect other government agencies such as the SEC, which may also impact our business by delaying review of our public filings, to the extent such review is necessary, and our ability to access the public markets.

We or the third parties upon whom we depend may be adversely affected by a natural disaster and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.

Natural disasters could severely disrupt our operations, and have a material adverse effect on our business, results of operations, financial condition and prospects. If a natural disaster, power outage or other event occurred that prevented us from using all or a significant portion of our headquarters, that damaged critical infrastructure, such as the manufacturing facilities of our third-party CMOs, or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. The disaster recovery and business continuity plans we have in place currently are limited and are unlikely to prove adequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which, could have a material adverse effect on our business, financial condition, results of operations and prospects.

We will continue to incur increased costs as a result of operating as a U.S.-listed public company, and our management will be required to devote substantial time to new compliance initiatives.

As a U.S. public company, and particularly now that we are no longer an emerging growth company, we have incurred and will continue to incur significant legal, accounting and other expenses that we did not incur as a public company listed on the LSE. In addition, the Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, and rules subsequently implemented by the SEC and Nasdaq have imposed various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel will need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will increase our legal and financial compliance costs and will make some activities more time-consuming and costly. For example, we expect that these rules and regulations may make it more difficult and more expensive for us to obtain director and officer liability insurance.

Pursuant to Section 404, we are required to furnish a report by our management on our internal control over financial reporting, including an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404, we have and continue to be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk we will not be able to conclude that our internal control over financial reporting is effective as required by Section 404. This could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

Risks Related to Our International Operations

As a company based in the United Kingdom, we are subject to economic, political, regulatory and other risks associated with international operations.

As a company based in the United Kingdom, our business is subject to risks associated with being organized outside of the United States. While the majority of our operations are in the United States and our functional

currency is the U.S. dollar, our future results could be harmed by a variety of international factors, including:

- economic weakness, including inflation, or political instability in particular non-U.S. economies and markets;
- differing and changing regulatory requirements;
- difficulties in compliance with different, complex and changing laws, regulations and court systems of multiple jurisdictions and compliance with a wide variety of foreign laws, treaties and regulations;
- changes in a specific country's or region's political or economic environment, including, but not limited to, the implications of one or more of the following occurring the decision of the United Kingdom:
- future activities subject to the terms of the Trade and Cooperation Agreement between the United Kingdom and the European Union effective May 1, 2021, which has not impacted our results to-date;
- a second referendum on Scottish independence from the United Kingdom; and/or
- a snap general election; and
- negative consequences from changes in tax laws.

Unfavorable global economic conditions, including conditions resulting from the COVID-19 pandemic, could adversely affect our business, financial condition or results of operations.

Our ability to invest in and expand our business and meet our financial obligations, to attract and retain third-party contractors and collaboration partners and to raise additional capital depends on our operating and financial performance, which, in turn, is subject to numerous factors, including the prevailing economic and political conditions and financial, business and other factors beyond our control, such as the rate of unemployment, the number of uninsured persons in the United States, political influences and inflationary pressures. For example, an overall decrease in or loss of insurance coverage among individuals in the United States as a result of unemployment, underemployment or the repeal of certain provisions of the ACA, may decrease the demand for healthcare services and pharmaceuticals. If fewer patients are seeking medical care because they do not have insurance coverage, we and our Founded Entities may experience difficulties in any eventual commercialization of the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates and our business, results of operations, financial condition and cash flows could be adversely affected.

In addition, our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets upon which pharmaceutical and biopharmaceutical companies such as us are dependent for sources of capital. In the past, global financial crises have caused extreme volatility and disruptions in the capital and credit markets. A severe or prolonged economic downturn could result in a variety of risks to our business, including a reduced ability to raise additional capital when needed on acceptable terms, if at all, and weakened demand for the therapeutic candidates within our Wholly Owned Pipeline. A weak or declining economy could also strain our suppliers, possibly resulting in supply disruption. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business.

The COVID-19 pandemic has had, and will continue to have, an unfavorable impact on global economic conditions, including a decrease in or loss of insurance coverage among individuals in the United States, an increase in unemployment, volatility in markets, and other negative impacts that have arisen or will arise over the course of the COVID-19 pandemic.

Our international operations may expose us to business, regulatory, political, operational, financial, pricing and reimbursement and economic risks associated with doing business outside of the United States.

Our business strategy incorporates potential international expansion to target patient populations outside the United States. If we or our Founded Entities receive regulatory approval for and commercialize any of the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates in patient populations outside the United States, we may hire sales representatives and conduct physician and patient association outreach activities outside of the United States. Doing business internationally involves a number of risks, including, but not limited to:

- multiple, conflicting, and changing laws and regulations such as privacy regulations, tax laws, export and import restrictions, employment laws, regulatory requirements, and other governmental approvals, permits, and licenses;
- failure by us to obtain and maintain regulatory approvals for the use of our therapeutics in various countries;
- additional potentially relevant third-party patent rights;
- complexities and difficulties in obtaining protection and enforcing our intellectual property;
- difficulties in staffing and managing foreign operations;
- complexities associated with managing multiple payor reimbursement regimes, government payors, or patient self-pay systems;
- limits in our ability to penetrate international markets;
- financial risks, such as longer payment cycles, difficulty collecting accounts receivable, the impact of local and regional financial crises on demand and payment for our therapeutics, and exposure to foreign currency exchange rate fluctuations;
- natural disasters, political and economic instability, including wars, such as the developing conflict between Russia and Ukraine, terrorism, and political unrest, outbreak of disease, boycotts, curtailment of trade, and other business restrictions;
- certain expenses including, among others, expenses for travel, translation, and insurance; and
- regulatory and compliance risks that relate to maintaining accurate information and control over sales and activities that may fall within the purview of the U.S. Foreign Corrupt Practices Act of 1977, as amended, or the FCPA, its books and records provisions, or its anti-bribery provisions.

Any of these factors could significantly harm our potential international expansion and operations and, consequently, our results of operations.

European data collection is governed by restrictive regulations governing the use, processing and cross-border transfer of personal information.

In the event we decide to conduct clinical trials or continue to enroll subjects in our ongoing or future clinical trials in the European Union, we may be subject to additional privacy restrictions. The collection and use of personal health data in the European Union is governed by the provisions of the General Data Protection Regulation (EU) 2016/679, or GDPR. This directive imposes several requirements relating to the consent of the individuals to whom the personal data relates, the information provided to the individuals, notification of data processing obligations to the competent national data protection authorities and the security and confidentiality of the personal data. The GDPR also imposes strict rules on the transfer of personal data out of the European Union to the United States. Failure to comply with the requirements of the Data Protection Directive, which governs the collection and use of personal health data in the European Union, the GDPR, and the related national data protection laws of the European Union Member States may result in fines and other administrative penalties. The GDPR introduced new data protection requirements in the European Union and substantial fines for breaches of the data protection rules. The GDPR regulations may impose additional responsibility and liability in relation to personal data that we process and we may be required to put in place additional mechanisms ensuring compliance with these and/or new data protection rules. This may be onerous and adversely affect our business, financial condition, prospects and results of operations.

We are subject to the U.K. Bribery Act 2010, or the Bribery Act, the U.S. Foreign Corrupt Practices Act of 1977 (as amended) ("FCPA") and other anti-corruption laws, as well as export control laws, import and customs laws, trade and economic sanctions laws and other laws governing our operations.

Our operations are subject to anti-corruption laws, including the Bribery Act, the FCPA, the U.S. domestic bribery statute contained in 18 U.S.C. §201, the U.S. Travel Act, and other anti-corruption laws that apply in countries where we do business. These laws generally prohibit us and our employees and intermediaries acting on our behalf from corruptly authorizing, promising, offering, or providing, directly or indirectly, anything else of value, to government officials or other persons to obtain or retain business or gain some other business advantage. The Bribery Act also prohibits: (i) "commercial" bribery of private parties, in addition to bribery involving domestic or foreign officials; (ii) the acceptance of bribes, as well as the giving of bribes, and (iii) "facilitation payments", meaning generally low level payments designed to secure or expedite routine governmental actions or other conduct to which persons are already under obligations to perform. The Bribery Act also creates an offence applicable corporate entities for failure to prevent bribery by our employees, officers, directors and other third parties acting on our behalf, to which the only defence is to maintain "adequate procedures" designed to prevent such acts of bribery.

In the future, we and our strategic partners may operate in jurisdictions that pose a heightened risk of potential Bribery Act or FCPA violations, and we may participate in collaborations and relationships with third parties whose conduct could potentially subject us to liability under the Bribery Act, FCPA or other anti-corruption laws, even if we do not explicitly authorize or have actual knowledge of such activities. In addition, we cannot predict the nature, scope or effect of future regulatory requirements to which our international operations might be subject or the manner in which existing laws might be administered or interpreted.

We are also subject to other laws and regulations governing our international operations, including regulations administered by the

governments of the United Kingdom and the United States, and authorities in the European Union and its member states, including applicable export control regulations, economic sanctions and embargoes on certain countries, regions, and persons, import and customs requirements and currency exchange regulations, collectively referred to as the Trade Control laws. Compliance with Trade Control Laws regarding the import and export of our products may create delays in the introduction of our products in international markets, and, in some cases, prevent the export of our products to some countries altogether.

There is no assurance that we will be completely effective in ensuring our compliance with all applicable anti-corruption laws, including the Bribery Act, the FCPA or other legal requirements, including Trade Control laws. If we are not in compliance with the Bribery Act, the FCPA and other anti-corruption laws or Trade Control laws, we may be subject to criminal and civil penalties, disgorgement, debarment from debarment from government contracts as well as other sanctions and remedial measures, and may also result in collateral litigation. These consequences could have an adverse impact on our business, financial condition, results of operations and liquidity. Likewise, any investigation of any potential violations of the Bribery Act, the FCPA, other anti-corruption laws or Trade Control laws by United Kingdom, United States or other authorities could also have an adverse impact on our reputation, our business, results of operations and financial condition. In addition, responding to any enforcement action may result in a significant diversion of management's attention and resources and significant defense costs and other professional fees.

The United Kingdom's withdrawal from the European Union may have a negative effect on global economic conditions, financial markets and our business, which could reduce the price of our ADSs.

On June 23, 2016, the United Kingdom held a referendum in which a majority of the eligible members of the electorate voted for the United Kingdom to leave the European Union. The United Kingdom's withdrawal from the European Union is commonly referred to as Brexit. In October 2019, a withdrawal agreement, or the Withdrawal Agreement, setting out the terms of the United Kingdom's exit from the European Union, and a political declaration on the framework for the future relationship between the United Kingdom and European Union was agreed between the UK and EU governments. Under the terms of the EU Withdrawal Agreement, the United Kingdom withdrew from membership of the European Union on 31 January 2020 and entered into a 'transition period', or the Transition Period, during which the majority of rights and obligations associated with membership of the European Union continued to apply to the United Kingdom; however, this expired on December 31, 2020. The United Kingdom and the European Union have signed a EU-UK Trade and Cooperation Agreement, which became provisionally applicable on January 1, 2021 and formally applicable effective May 1, 2021. This agreement provides details on how some aspects of the United Kingdom and European Union's relationship will operate going forwards however there are still many uncertainties.

These developments have had and may continue to have a significant adverse effect on global economic conditions and the stability of global financial markets, and could significantly reduce global market liquidity and restrict the ability of key market participants to operate in certain financial markets. In particular, it could also lead to a period of considerable uncertainty in relation to the UK financial and banking markets. As a result of this uncertainty, global financial markets could experience significant volatility, which could adversely affect the market price of our ADSs. Asset valuations, currency exchange rates and credit ratings may also be subject to increased market volatility.

We may also face new regulatory costs and challenges that could have an adverse effect on our operations. The United Kingdom will lose the benefits of global trade agreements negotiated by the European Union on behalf of its members, which may result in increased trade barriers that could make our doing business in Europe more difficult. In addition, currency exchange rates in the pound sterling and the euro with respect to each other and the U.S. dollar have already been adversely affected by Brexit. Furthermore, now that the Transition Period has expired, Great Britain will no longer be covered by the centralized procedure for obtaining EEA-wide marketing authorization from the EMA and a separate process for authorization of drug therapeutics, including the therapeutic candidates within our Wholly Owned Pipeline, will be required in Great Britain, resulting in an authorization covering the United Kingdom or Great Britain only. For a period of two years from January 1, 2021, the Medicines and Healthcare products Regulatory Agency, or MHRA (the UK medicines and medical devices regulator) may rely on a decision taken by the European Commission on the approval of a new marketing authorization in the centralized procedure, in order to more quickly grant a Great Britain marketing authorization. A separate application will, however, still be required. The MHRA has published a series of guidance notes on how the process for authorization of medicines will now work, however exactly what implications this will have in practice remain unclear.

Risks Related to Our Equity Securities and ADSs

The market price of our ADSs has been and will likely continue to be highly volatile, and you could lose all or part of your investment.

The market price of our ADSs has been and will likely continue to be volatile. The stock market in general, and the market for biopharmaceutical companies in particular, has experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, you may not be able to sell your ADSs at or above the purchase price. The market price for our ADSs may be influenced by many factors, including:

- adverse results or delays in our preclinical studies or clinical trials;
- reports of AEs or other negative results in clinical trials of third parties' therapeutic candidates that target the therapeutic candidates within our Wholly Owned Pipeline's or our Founded Entities' therapeutic candidates' target indications;
- an inability for us to obtain additional funding on reasonable terms or at all;
- any delay in submitting an IND, BLA or NDA for the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates and any adverse development or perceived adverse development with respect to the FDA's review of that IND, BLA or NDA;
- failure to develop successfully and commercialize the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates;
- announcements we make regarding our current therapeutic candidates, acquisition of potential new therapeutic candidates and companies and/or in-licensing;
- failure to maintain our or our Founded Entities' existing license arrangements or enter into new licensing and collaboration agreements;
- failure by us, our Founded Entities or our licensors to prosecute, maintain or enforce our intellectual property rights;
- changes in laws or regulations applicable to future therapeutics;
- inability to obtain adequate clinical or commercial supply for the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates or the inability to do so at acceptable prices;
- adverse regulatory decisions, including failure to reach agreement with applicable regulatory authorities on the design or scope of our planned clinical trials;
- failure to obtain and maintain regulatory exclusivity for the therapeutic candidates within our Wholly Owned Pipeline or our Founded Entities' therapeutic candidates;
- regulatory approval or commercialization of new therapeutics or other methods of treating our target disease indications by our competitors;
- failure to meet or exceed financial projections we may provide to the public or to the investment community;
- publication of research reports or comments by securities or industry analysts;
- the perception of the pharmaceutical and biotechnology industries by the public, legislatures, regulators and the investment community;
- announcements of significant acquisitions, strategic partnerships, joint ventures or capital commitments by us, our Founded Entities our strategic collaboration partners or our competitors;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our or our Founded Entities' ability to obtain patent protection for our technologies;
- additions or departures of our key scientific or management personnel;
- significant lawsuits, including patent or shareholder litigation, against us;
- changes in the market valuations of similar companies;
- adverse developments relating to any of the above or additional factors with respect to our Founded Entities;
- sales or potential sales of substantial amounts of our ADSs; and
- trading volume of our ADSs.

In addition, companies trading in the stock market in general, and Nasdaq, in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may negatively affect the market price of our ADSs, regardless of our actual operating performance. Since our ADSs were initially sold in November 2020 at a price of $33.00 per ADS, our ADS price has fluctuated significantly, ranging from an intraday low of $21.95 to an intraday high of $63.95 for the period beginning November 16, 2020, our first day of trading on The Nasdaq Global Market, through March 31, 2022. If the market price of our ADSs does not exceed the price at which you acquired them, you may not

realize any return on your investment in us and may lose some or all of your investment.

If securities or industry analysts do not publish research or publish inaccurate or unfavorable research about our business, our ADS price and trading volume could decline.

The trading market for our ADSs and ordinary shares depends in part on the research and reports that securities or industry analysts publish about us or our business. If no or few securities or industry analysts cover our company, the trading price for our ADSs and ordinary shares would be negatively impacted. If one or more of the analysts who covers us downgrades our equity securities or publishes incorrect or unfavorable research about our business, the price of our ordinary shares and ADSs would likely decline. If one or more of these analysts ceases coverage of our company or fails to publish reports on us regularly, or downgrades our securities, demand for our ordinary shares and ADSs could decrease, which could cause the price of our ordinary shares and ADSs or their trading volume to decline.

Future sales, or the possibility of future sales, of a substantial number of our securities could adversely affect the price of the shares and dilute shareholders.

Sales of a substantial number of our ADSs in the public market could occur at any time, subject to certain restrictions described below. If our existing shareholders sell, or indicate an intent to sell, substantial amounts of our securities in the public market, the trading price of the ADSs could decline significantly and could decline below the original purchase price. As of March 31, 2022, we had 287,841,508 outstanding ordinary shares. Ordinary shares subject to outstanding options under our equity incentive plans and the ordinary shares reserved for future issuance under our equity incentive plans will become eligible for sale in the public market in the future, subject to certain legal and contractual limitations.

Holders of ADSs are not treated as holders of our ordinary shares.

If you purchase an ADS, you will become a holder of ADSs with underlying ordinary shares in a company incorporated under English law. Holders of ADSs are not treated as holders of our ordinary shares, unless they withdraw the ordinary shares underlying their ADSs in accordance with the deposit agreement and applicable laws and regulations. The depositary is the holder of the ordinary shares underlying the ADSs. Holders of ADSs therefore do not have any rights as holders of our ordinary shares, other than the rights that they have pursuant to the deposit agreement. See "Description of Securities Other Than Equity Securities" in our Annual Report on Form 20-F.

Holders of ADSs may be subject to limitations on the transfer of their ADSs and the withdrawal of the underlying ordinary shares.

ADSs are transferable on the books of the depositary. However, the depositary may close its books at any time or from time to time when it deems expedient in connection with the performance of its duties. The depositary may refuse to deliver, transfer or register transfers of ADSs generally when our books or the books of the depositary are closed, or at any time if we or the depositary think it is advisable to do so because of any requirement of law, government or governmental body, or under any provision of the deposit agreement, or for any other reason, subject to the right of ADS holders to cancel their ADSs and withdraw the underlying ordinary shares. Temporary delays in the cancellation of your ADSs and withdrawal of the underlying ordinary shares may arise because the depositary has closed its transfer books or we have closed our transfer books, the transfer of ordinary shares is blocked to permit voting at a shareholders' meeting or we are paying a dividend on our ordinary shares. In addition, ADS holders may not be able to cancel their ADSs and withdraw the underlying ordinary shares when they owe money for fees, taxes and similar charges and when it is necessary to prohibit withdrawals in order to comply with any laws or governmental regulations that apply to ADSs or to the withdrawal of ordinary shares or other deposited securities. See "Description of Securities Other Than Equity Securities" in our Annual Report on Form 20-F.

ADS holders may not be entitled to a jury trial with respect to claims arising under the deposit agreement, which could result in less favorable outcomes to the plaintiff(s) in any such action.

The deposit agreement governing the ADSs representing our ordinary shares provides that, to the fullest extent permitted by law, holders and beneficial owners of ADSs irrevocably waive the right to a jury trial of any claim they may have against us or the depositary arising out of or relating to the ADSs or the deposit agreement.

If this jury trial waiver provision is not permitted by applicable law, an action could proceed under the terms of the deposit agreement with a jury trial. If we or the depositary opposed a jury trial demand based on the waiver, the court would determine whether the waiver was enforceable based on the facts and circumstances of that case in accordance with the applicable state and federal law. To our knowledge, the enforceability of a contractual pre-dispute jury trial waiver in connection with claims arising under the federal securities laws has not been finally adjudicated by the U.S. Supreme Court. However, we believe that a contractual pre-dispute jury trial waiver provision is generally enforceable, including under the laws of the State of New York, which govern the deposit agreement, by a federal or state court in the City of New York, which has non-exclusive jurisdiction over matters arising under the deposit agreement. In determining whether to enforce a contractual pre-dispute jury trial waiver provision, courts will generally consider whether a party knowingly, intelligently and voluntarily waived the right to a jury trial. We believe that this is the case with respect to the deposit agreement and the ADSs. It is advisable that you consult legal counsel regarding the jury waiver provision before entering into the deposit agreement.

If you or any other holders or beneficial owners of ADSs bring a claim against us or the depositary in connection with matters arising under the deposit agreement or the ADSs, including claims under federal securities laws, you or such other holder or beneficial owner may not be entitled to a jury trial with respect to such claims, which may have the effect of limiting and discouraging lawsuits against us and/or the depositary. If a lawsuit is brought against us and/or the depositary under the deposit agreement, it may be heard only by a judge or justice of the applicable trial court, which would be conducted according to different civil procedures and may result in different outcomes than a trial by jury would have had, including results that could be less favorable to the plaintiff(s) in any such action, depending on, among other things, the nature of the claims, the judge or justice hearing such claims, and the venue of the hearing.

No condition, stipulation or provision of the deposit agreement or ADSs serves as a waiver by any holder or beneficial owner of ADSs or by us or the depositary of compliance with the U.S. federal securities laws and the rules and regulations promulgated thereunder.

One of our principal shareholders has a significant holding in the company which may give them influence in certain matters requiring approval by shareholders, including approval of significant corporate transactions in certain circumstances.

As of February 16, 2022, Invesco Asset Management Limited, or Invesco, held approximately 22.5 percent of our ordinary shares. Accordingly, Invesco may, as a practical matter, be able to influence certain matters requiring approval by shareholders, including approval of significant corporate transactions in certain circumstances. Such concentration of ownership may also have the effect of delaying or preventing any future proposed change in control of the Company. The trading price of the ordinary shares could be adversely affected if potential new investors are disinclined to invest in the Company because they perceive disadvantages to a large shareholding being concentrated in the hands of a single shareholder. The interests of Invesco and the investors that acquire ADSs may not be aligned. Invesco may make acquisitions of, or investments in, other businesses in the same sectors as us or our Founded Entities. These businesses may be, or may become, competitors of us or our Founded Entities. In addition, funds or other entities managed or advised by Invesco may be in direct competition with us or our Founded Entities on potential acquisitions of, or investments in, certain businesses. In addition, Invesco holds equity interests in certain of our Founded Entities where they may exert direct influence.

You will not have the same voting rights as the holders of our ordinary shares and may not receive voting materials in time to be able to exercise your right to vote.

Except as described in our Annual Report on Form 20-F and the deposit agreement, holders of the ADSs will not be able to exercise voting rights attaching to the ordinary shares represented by the ADSs. Under the terms of the deposit agreement, holders of the ADSs may instruct the depositary to vote the ordinary shares underlying their ADSs. Otherwise, holders of ADSs will not be able to exercise their right to vote unless they withdraw the ordinary shares underlying their ADSs to vote them in person or by proxy in accordance with applicable laws and regulations and our Articles of Association. Even so, ADS holders may not know about a meeting far enough in advance to withdraw those ordinary shares. If we ask for the instructions of holders of the ADSs, the depositary, upon timely notice from us, will notify ADS holders of the upcoming vote and arrange to deliver our voting materials to them. Upon our request, the depositary will mail to holders a shareholder meeting notice that contains, among other things, a statement as to the manner in which voting instructions may be given. We cannot guarantee that ADS holders will receive the voting materials in time to ensure that they can instruct the depositary to vote the ordinary shares underlying their ADSs. A shareholder is only entitled to participate in, and vote at, the meeting of shareholders, provided that it holds our ordinary shares as of the record date set for such meeting and otherwise complies with our Articles of Association. In addition, the depositary's liability to ADS holders for failing to execute voting instructions or for the manner

of executing voting instructions is limited by the deposit agreement. As a result, holders of ADSs may not be able to exercise their right to give voting instructions or to vote in person or by proxy and they may not have any recourse against the depositary or us if their ordinary shares are not voted as they have requested or if their shares cannot be voted.

You may not receive distributions on our ordinary shares represented by the ADSs or any value for them if it is illegal or impractical to make them available to holders of ADSs.

The depositary for the ADSs has agreed to pay to you any cash dividends or other distributions it or the custodian receives on our ordinary shares or other deposited securities after deducting its fees and expenses. You will receive these distributions in proportion to the number of our ordinary shares your ADSs represent. However, in accordance with the limitations set forth in the deposit agreement, it may be unlawful or impractical to make a distribution available to holders of ADSs. We have no obligation to take any other action to permit distribution on the ADSs, ordinary shares, rights or anything else to holders of the ADSs. This means that you may not receive the distributions we make on our ordinary shares or any value from them if it is unlawful or impractical to make them available to you. These restrictions may have an adverse effect on the value of your ADSs.

Because we do not have immediate plans to pay any cash dividends on our ADSs, capital appreciation, if any, may be your sole source of gains and you may never receive a return on your investment.

Under current English law, a company's accumulated realized profits must exceed its accumulated realized losses (on a non-consolidated basis) before dividends can be declared and paid. Therefore, we must have sufficient distributable profits before declaring and paying a dividend. We have not paid dividends in the past on our ordinary shares. We have not announced any immediate plans to pay any cash dividends. As a result, capital appreciation, if any, on our ADSs will be your sole source of gains for the foreseeable future, and you would suffer a loss on your investment if you were unable to sell your ADSs at or above the price that you initially paid for them. Investors seeking cash dividends should not purchase our ADSs.

Risks Related to Our Corporate Status

We are no longer an "emerging growth company" and, as a result, are subject to certain enhanced disclosure requirements.

Because the market value of our equity securities held by non-affiliates exceeded $700.0 million as of June 30, 2021, among other things, we no longer qualified as an emerging growth company as of December 31, 2021. As a result, we are subject to certain requirements that apply to other public companies but did not previously apply to us due to our status as an emerging growth company, such as the auditor attestation requirements under Section 404 of the Sarbanes Oxley Act. Compliance with these enhanced disclosure requirements will increase our costs and could negatively affect our results of operations and financial condition.

We are not, and do not intend to become, regulated as an "investment company" under the Investment Company Act of 1940, as amended, or the 1940 Act and if we were deemed an "investment company" under the 1940 Act, applicable restrictions could make it impractical for us to continue our business as contemplated and could have a material adverse effect on our business.

The 1940 Act and the rules thereunder contain detailed parameters for the organization and operation of investment companies. Among other things, the 1940 Act and the rules thereunder limit or prohibit transactions with affiliates, impose limitations on the issuance of debt and equity securities and impose certain governance requirements. We have not been and do not intend to become regulated as an investment company, and we intend to conduct our activities so that we will not be deemed to be an investment company under the 1940 Act. In order to ensure that we are not deemed to be an investment company, we may be limited in the assets that we may continue to own and, further, may need to dispose of or acquire certain assets at such times or on such terms as may be less favorable to us than in the absence of such requirement. If anything were to happen which would cause us to be deemed to be an investment company under the 1940 Act (such as significant changes in the value of our Founded Entities or a change in circumstance that results in a reclassification of our interests in our Founded Entities for purposes of the 1940 Act), the requirements imposed by the 1940 Act could make it impractical for us to continue our business as currently conducted, which would materially adversely affect our business, results of operations and financial condition. In addition, if we were to become inadvertently subject to the 1940 Act, any violation of the 1940 Act could subject us to material adverse consequences, including potentially significant regulatory penalties and the possibility that certain of our contracts could be deemed unenforceable.

As a foreign private issuer, we are exempt from a number of rules under the U.S. securities laws and are permitted to file less information with the SEC than a U.S. company. This may limit the information available to holders of ADSs or our ordinary shares.

We are a "foreign private issuer," as defined in the SEC's rules and regulations and, consequently, we are not subject to all of the disclosure requirements applicable to public companies organized within the United States. For example, we are exempt from certain rules under the Exchange Act, that regulate disclosure obligations and procedural requirements related to the solicitation of proxies, consents or authorizations applicable to a security registered under the Exchange Act, including the U.S. proxy rules under Section 14 of the Exchange Act. In addition, our officers and directors are exempt from the reporting and "short-swing" profit recovery provisions of Section 16 of the Exchange Act and related rules with respect to their purchases and sales of our securities. Moreover, while we currently make annual and semi-annual filings with respect to our listing on the LSE, we will not be required to file periodic reports and financial statements with the SEC as frequently or as promptly as U.S. domestic issuers and will not be required to file quarterly reports on Form 10-Q or current reports on Form 8-K under the Exchange Act. Accordingly, there will be less publicly available information concerning our company than there would be if we were not a foreign private issuer.

As a foreign private issuer, we are permitted to adopt certain home country practices in relation to corporate governance matters that differ significantly from Nasdaq corporate governance listing standards. These practices may afford less protection to shareholders than they would enjoy if we complied fully with corporate governance listing standards.

As a foreign private issuer listed on Nasdaq, we are subject to corporate governance listing standards. However, rules permit a foreign private issuer like us to follow the corporate governance practices of its home country. Certain corporate governance practices in the United Kingdom, which is our home country, may differ significantly from corporate governance listing standards. For example, neither the corporate laws of the United Kingdom nor our articles of association require a majority of our directors to be independent and we could include non-independent directors as members of our nomination and remuneration committee, though a majority is required, and our independent directors would not necessarily hold regularly scheduled meetings at which only independent directors are present. Currently, we follow home country practice to the maximum extent possible. Therefore, our shareholders may be afforded less protection than they otherwise would have under corporate governance listing standards applicable to U.S. domestic issuers. See "Governance" of this Annual Report and Accounts and "Item 16G—Corporate Governance" of our Annual Report on Form 20-F,

We may lose our foreign private issuer status in the future, which could result in significant additional cost and expense.

While we currently qualify as a foreign private issuer, the determination of foreign private issuer status is made annually on the last business day of an issuer's most recently completed second fiscal quarter and, accordingly, the next determination will be made with respect to us on June 30, 2022.

In the future, we would lose our foreign private issuer status if we to fail to meet the requirements necessary to maintain our foreign private issuer status as of the relevant determination date. For example, if more than 50 percent of our securities are held by U.S. residents and more than 50 percent of the members of our executive committee or members of our board of directors are residents or citizens of the United States, we could lose our foreign private issuer status.

The regulatory and compliance costs to us under U.S. securities laws as a U.S. domestic issuer may be significantly more than costs we incur as a foreign private issuer. If we are not a foreign private issuer, we will be required to file periodic reports and registration statements on U.S. domestic issuer forms with the SEC, which are more detailed and extensive in certain respects than the forms available to a foreign private issuer. We would be required under current SEC rules to prepare our financial statements in accordance with U.S. GAAP, rather than IFRS, and modify certain of our policies to comply with corporate governance practices associated with U.S. domestic issuers. Such conversion of our financial statements to U.S. GAAP will involve significant time and cost. In addition, we may lose our ability to rely upon exemptions from certain corporate governance requirements on U.S. stock exchanges that are available to foreign private issuers such as the ones described above and exemptions from procedural requirements related to the solicitation of proxies.

Risks Related to Our Internal Controls

We have identified a material weakness in our internal control over financial reporting in connection with the audit of our consolidated financial statements in accordance with the standards of the PCAOB and U.S. securities laws. If we fail to implement and maintain effective internal control over financial reporting, we may be unable to accurately report our results of operations, meet our reporting obligations or prevent fraud.

Section 404 of the Sarbanes-Oxley Act requires that our management assess our internal control over financial reporting and that we include a report of management on our internal control over financial reporting in our annual reports on Form 20-F. As disclosed in more detail under Item 15 "Controls and Procedures" of this Report, we have concluded that our internal control over financial reporting was ineffective as of December 31, 2021 due to a material weakness that was unremediated as of December 31, 2021 and is described in Item 15.

A material weakness is a deficiency, or combination of control deficiencies, in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of the annual or interim financial statements will not be prevented or detected on a timely basis. The material weakness relates to our risk assessment process over the design and implementation of our management review controls over the valuation of financial instruments, the completeness and accuracy of related sensitivity disclosures, the valuation of share based payment liabilities and completeness and the accuracy of the tax provision. There was insufficient precision in and documentation of the performance of such review controls resulting in controls not being designed in a way to sufficiently address the level of aggregation and criteria for investigation. Additionally, management did not completely identify the information used in the control and did not design sufficient controls to address the relevance and reliability of such information. We concluded that a similar material weakness existed as of December 31, 2020, and this material weakness continued to exist at December 31, 2021. We intend to take further steps to implement our remediation plan, including the implementation of more robust procedures to identify and document relevant risks at an appropriately disaggregated level and more detailed management review controls to mitigate such risks. While we expect to continue to implement our remediation plan through 2022, we cannot be certain as to when remediation will be fully completed. As with any internal control framework, we cannot be certain that these efforts will be sufficient to remediate our material weakness or prevent future material weaknesses or significant deficiencies from occurring in the future. If we are unable to successfully remediate our existing or any future material weaknesses in our internal control over financial reporting, or if we identify any additional material weaknesses, the accuracy and timing of our financial reporting may be adversely affected.

Effective internal control over financial reporting is necessary for us to provide reliable financial reports and, together with adequate disclosure controls and procedures, are designed to prevent fraud. Any failure to implement or maintain these controls, or difficulties encountered in their implementation, could cause us to fail to meet our reporting obligations. In addition, any testing by us or by our independent registered public accounting firm may reveal additional deficiencies in our internal control over financial reporting that are deemed to be material weaknesses or that may require prospective or retroactive changes to our financial statements or identify other areas for further attention or improvement.

If we fail to achieve and maintain effective internal control over financial reporting, we could suffer material misstatements in our financial statements and fail to meet our reporting obligations, which could cause investors to lose confidence in our reported financial information. This could in turn limit our access to capital markets or lead to a decline in the trading price of our securities. We may also be required to restate our financial statements from prior periods. Additionally, ineffective internal control over financial reporting could expose us to increased risk of fraud or misuse of corporate assets and subject us to potential delisting from the stock exchange on which we list, regulatory investigations, litigation from shareholders and civil or criminal sanctions, which could have a material adverse effect on our business.

Our disclosure controls and procedures may not prevent or detect all errors or acts of fraud.

We are subject to certain reporting requirements of the Exchange Act. Our disclosure controls and procedures are designed to reasonably assure that information required to be disclosed by us in reports we file or submit under the Exchange Act is accumulated and communicated to management, recorded, processed, summarized and reported within the time periods specified in the rules and forms of the SEC. We believe that any disclosure controls and procedures or internal controls and procedures, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. These inherent limitations include the realities that judgments in decision-making can be faulty, and that breakdowns can occur because of simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by an unauthorized override of the controls. Accordingly, because of the inherent limitations in our control system, misstatements or insufficient disclosures due to error or fraud may occur and not be detected.

Risks Related to Tax Matters

Comprehensive tax reform legislation could adversely affect our business and financial condition.

The rules dealing with U.S. federal, state, and local income taxation are constantly under review by persons involved in the legislative process and by the Internal Revenue Service and the U.S. Treasury Department. Changes to tax laws (which changes may have retroactive application) could adversely affect us or holders of our common stock. In recent years, many such changes have been made and changes are likely to continue to occur in the future. For example, on December 22, 2017, the Tax Act was signed into law and enacted many significant changes to U.S. tax laws. Future guidance from the Internal Revenue Service and other tax authorities with respect to the Tax Act may affect us, and certain aspects of the Tax Act could be repealed or modified in future legislation. For example, on March 27, 2020, the "Coronavirus Aid, Relief, and Economic Security Act" or the CARES Act was signed into law, which modified certain provisions of the Tax Act and included certain changes in tax law intended to stimulate the U.S. economy in light of the COVID-19 coronavirus outbreak, including temporary beneficial changes to the treatment of net operating losses, interest deductibility limitations and payroll tax matters. It is uncertain if and to what extent various states will conform to the newly enacted federal tax law. We will continue to examine the impact tax reform legislation may have on our business.

We are treated as a U.S. domestic corporation for U.S. federal income tax purposes.

We are treated as a U.S. domestic corporation for U.S. federal income tax purposes under Section 7874(b) of the Internal Revenue Code of 1986, as amended, or the Code. As a result, we are subject to U.S. income tax on our worldwide income and any dividends paid by us to non-U.S. holders (as defined in the discussion under "Taxation in the United States" in our Annual Report on Form 20-F) will be subject to U.S. federal income tax withholding at a 30 percent rate or such lower rate as provided in an applicable treaty. Furthermore, PureTech Health plc is also resident for tax purposes in the U.K. and subject to U.K. corporation tax on its worldwide income and gains. Consequently, we may be liable for both U.S. and U.K. income tax, which could have a material adverse effect on our financial condition and results of operations.

This discussion of certain U.S. federal income tax risks is subject in its entirety to the summaries set forth in "Certain United Kingdom Tax Considerations" and "Taxation in the United States" in our Annual Report on Form 20-F

Our ability to use our net operating losses to offset future taxable income may be subject to certain limitations.

As of December 31, 2021, we had U.S. federal and state net operating loss carryforwards, or NOLs, of approximately $215.3 million and 27.9 million respectively, due to prior period losses, which, subject to the following discussion, are generally available to be carried forward to offset our future taxable income, if any, until such NOLs are used or expire. In general, under Section 382 of the Code, a corporation that undergoes an "ownership change," generally defined as a greater than 50 percentage point change (by value) in its equity ownership by certain shareholders over a three year period, is subject to limitations on its ability to utilize its NOLs to offset future taxable income. Our existing NOLs may be subject to limitations arising from previous ownership changes, and if we undergo an ownership change, our ability to utilize NOLs could be further limited by Section 382 of the Code. Future changes in our stock ownership, some of which are outside of our control, could result in an ownership change under Section 382 of the Code. Additionally, we may no longer be able to utilize losses of our Founded Entities that have been deconsolidated or that will deconsolidate in the future. Furthermore, our ability to utilize NOLs of companies that we have acquired or may acquire in the future may be subject to limitations. In addition, under the Tax Act, the amount of post 2017 NOLs that we are permitted to deduct in any taxable year is limited to the lesser of our NOLs or 80 percent of our taxable income in such year (subject to Section 382 of the Code), where taxable income is determined without regard to the NOL deduction itself. Federal NOLs generated after December 31, 2017 are not subject to expiration and generally may not be carried back to prior taxable years, except that under the CARES Act, NOLs generated in 2018, 2019 and 2020 may be carried back five taxable years and these NOLs could fully offset prior year taxable income without the 80% taxable income limitation under the CARES Act.. There is also a risk that due to regulatory changes, such as suspensions on the use of NOLs, or other unforeseen reasons, our existing NOLs could be unavailable to offset future income tax liabilities. In addition, changes under the Tax Act,

as amended by the CARES Act, includes changes to the U.S. federal tax rates and the rules governing NOLs that may significantly impact our ability to utilize our NOLs to offset taxable income in the future. For these reasons, we may not be able to realize a tax benefit from the use of our NOLs.

We may be unable to use net operating loss and tax credit carryforwards and certain built-in losses to reduce future U.K. tax liabilities.

As a U.K. incorporated and tax resident entity, PureTech Health plc is subject to U.K. corporate taxation on its tax-adjusted trading profits. Due to the nature of our business, PureTech Health plc has generated losses since inception and therefore we have not paid any U.K. corporation tax. Subject to numerous utilization criteria and restrictions (including those that limit the percentage of profits that can be reduced by carried forward losses and those that can restrict the use of carried forward losses where there is a change of ownership of more than half the ordinary shares of the company and a major change in the nature, conduct or scale of the trade), we expect these to be eligible for carry forward and utilization against future U.K. operating profits.

Future changes to tax laws could materially adversely affect our company and reduce net returns to our shareholders.

The tax treatment of the company is subject to changes in tax laws, regulations and treaties, or the interpretation thereof, tax policy initiatives and reforms under consideration and the practices of tax authorities in jurisdictions in which we operate, as well as tax policy initiatives and reforms related to the Organisation for Economic Co-Operation and Development's, or OECD, Base Erosion and Profit Shifting, or BEPS, Project, the European Commission's state aid investigations and other initiatives. Such changes may include (but are not limited to) the taxation of operating income, investment income, dividends received or (in the specific context of withholding tax) dividends paid. We are unable to predict what tax reform may be proposed or enacted in the future or what effect such changes would have on our business, but such changes, to the extent they are brought into tax legislation, regulations, policies or practices, could affect our financial position and overall or effective tax rates in the future in countries where we have operations, reduce post-tax returns to our shareholders, and increase the complexity, burden and cost of tax compliance.

Tax authorities may disagree with our positions and conclusions regarding certain tax positions, resulting in unanticipated costs, taxes or non-realization of expected benefits.

A tax authority may disagree with tax positions that we have taken, which could result in increased tax liabilities. For example, HM Revenue & Customs, or HMRC, the Internal Revenue Service or another tax authority could challenge our allocation of income by tax jurisdiction and the amounts paid between certain of our Founded Entities pursuant to our intercompany arrangements and transfer pricing policies, including amounts paid with respect to our intellectual property development. Similarly, a tax authority could assert that we are subject to tax in a jurisdiction where we believe we have not established a taxable connection, often referred to as a "permanent establishment" under international tax treaties, and such an assertion, if successful, could increase our expected tax liability in one or more jurisdictions. A tax authority may take the position that material income tax liabilities, interest and penalties are payable by us, in which case, we expect that we might contest such assessment. Contesting such an assessment may be lengthy and costly and if we were unsuccessful in disputing the assessment, the implications could increase our anticipated effective tax rate, where applicable.

Shareholder protections found in provisions under the U.K. City Code on Takeovers and Mergers, or the Takeover Code, will not apply if our securities are no longer admitted to trading on a regulated market or a multilateral trading facility in the United Kingdom or on any stock exchange in the Channel Islands or the Isle of Man and our place of management and control is considered to change to outside the United Kingdom.

We are registered as a public limited company incorporated in England and Wales and have our ordinary shares admitted to trading on a regulated market in the United Kingdom (being the main market of the LSE). Accordingly, we are currently subject to the Takeover Code and, as a result, our shareholders are entitled to the benefit of certain takeover offer protections provided under the Takeover Code. The Takeover Code provides a framework within which takeovers of companies are regulated and conducted. If, at the time of a takeover offer, we have de-listed from the main market of the LSE (and do not maintain a listing of securities on any other regulated market or a multilateral trading facility in the United Kingdom or on any stock exchange in the Channel Islands or the Isle of Man) and the Panel on Takeovers and Mergers determine that we do not have our place of central management and control in the United Kingdom, then the Takeover Code may not apply to us and our shareholders would not be entitled to the benefit of the various protections that the Takeover Code affords. In particular, we would not be subject to the rules regarding mandatory takeover bids. The following is a brief summary of some of the most important rules of the Takeover Code:

- when any person acquires, whether by a series of transactions over a period of time or not, an interest in shares which (taken together with shares already held by that person and an interest in shares held or acquired by persons acting in concert with him or her) carry 30 percent or more of the voting rights of a company that is subject to the Takeover Code, that person is generally required to make a mandatory offer to all the holders of any class of equity share capital or other class of transferable securities carrying voting rights in that company to acquire the balance of their interests in the company;
- when any person who, together with persons acting in concert with him or her, is interested in shares representing not less than 30 percent but does not hold more than 50 percent of the voting rights of a company that is subject to the Takeover Code, and such person, or any person acting in concert with him or her, acquires an additional interest in shares which increases the percentage of shares carrying voting rights in which he or she is interested, then such person is generally required to make a mandatory offer to all the holders of any class of equity share capital or other class of transferable securities carrying voting rights of that company to acquire the balance of their interests in the company;
- a mandatory offer triggered in the circumstances described in the two paragraphs above must be in cash (or be accompanied by a cash alternative) and at not less than the highest price paid within the preceding 12 months to acquire any interest in shares in the company by the person required to make the offer or any person acting in concert with him or her;
- in relation to a voluntary offer (i.e. any offer which is not a mandatory offer), when interests in shares representing 10 percent or more of the shares of a class have been acquired for cash by an offeror (i.e., a bidder) and any person acting in concert with it in the offer period and the previous 12 months, the offer must be in cash or include a cash alternative for all shareholders of that class at not less than the highest price paid for any interest in shares of that class by the offeror and by any person acting in concert with it in that period. Further, if an offeror acquires for cash any interest in shares during the offer period, a cash alternative must be made available at not less than the highest price paid for any interest in the shares of that class;
- if the offeror acquires an interest in shares in an offeree company (i.e., a target) at a price higher than the value of the offer, the offer must be increased to not less than the highest price paid for the interest in shares so acquired;
- the offeree company must obtain competent advice as to whether the terms of any offer are fair and reasonable and the substance of such advice must be made known to all the shareholders, together with the opinion of the board of directors of the offeree company;
- special or favorable deals for selected shareholders are not permitted, except in certain circumstances where independent shareholder approval is given and the arrangements are regarded as fair and reasonable in the opinion of the financial adviser to the offeree;
- all shareholders must be given the same information;
- each document published in connection with an offer by or on behalf of the offeror or offeree must state that the directors of the offeror or the offeree, as the case may be, accept responsibility for the information contained therein;
- profit forecasts, quantified financial benefits statements and asset valuations must be made to specified standards and must be reported on by professional advisers;
- misleading, inaccurate or unsubstantiated statements made in documents or to the media must be publicly corrected immediately;
- actions during the course of an offer by the offeree company, which might frustrate the offer are generally prohibited unless shareholders approve these plans. Frustrating actions would include, for example, lengthening the notice period for directors under their service contract or agreeing to sell off material parts of the target group;
- stringent and detailed requirements are laid down for the disclosure of dealings in relevant securities during an offer, including the prompt disclosure of positions and dealing in relevant securities by the parties to an offer and any person who is interested (directly or indirectly) in 1 percent or more of any class of relevant securities; and
- employees of both the offeror and the offeree company and the trustees of the offeree company's pension scheme must be informed about an offer. In addition, the offeree company's employee representatives and pension scheme trustees have the right to have a separate opinion on the effects of the offer on employment appended to the offeree board of directors' circular or published on a website.

Company information

Directors, Secretary and Advisors to PureTech

Company Registration Number
09582467

Registered Office
8th Floor
20 Farringdon Street
London EC4A 4AB
United Kingdom

Website
www.puretechhealth.com

Board of Directors
Mr. Christopher Viehbacher (Chair)
Ms. Daphne Zohar (Chief Executive Officer)
Dame Marjorie Scardino
(Senior Independent Non-Executive Director)
Dr. Robert Langer (Non-Executive Director)
Dr. Raju Kucherlapati
(Independent Non-Executive Director)
Dr. John LaMattina (Independent
Non-Executive Director)
Ms. Kiran Mazumdar-Shaw
(Independent Non-Executive Director)
Ms. Sharon Barber-Lui
(Independent Non-Executive Director)
Dr. Bharatt Chowrira
(President and Chief Business,
Legal & Operating Officer)

Company Secretary
Dr. Bharatt Chowrira

Media and Public Relations
FTI Consulting, Inc.
200 Aldersgate
Aldersgate Street
London EC1A 4HD
United Kingdom

Tel: +44 203 727 1000

Independent Auditor
KPMG LLP
15 Canada Square
London E14 5GL
United Kingdom

Tel: +44 207 311 1000

Broker
Jefferies International Limited
100 Bishopsgate
London EC2N 4JL
United Kingdom

Tel: +44 207 029 8000

Registrar
Computer Share Investor Services PLC
The Pavilions
Bridgwater Road
Bristol BS99 6ZY
United Kingdom

Tel: +44 (0)370 707 1147

Solicitors
DLA Piper UK LLP
160 Aldersgate Street
London EC1A 4HT
United Kingdom

Tel: +44 870 011 1111

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PureTech Health
6 Tide Street
Suite 400
Boston
MA 02210

Tel: +1 617 482 2333
Email: info@puretechhealth.com