UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 10-K

(Mark One)

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the fiscal year ended December 31, 2022

or

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the transition period from to

Commission File No. 001-38959

BridgeBio Pharma, Inc.
(Exact name of registrant as specified in its charter)

Delaware	**84-1850815**
State or other jurisdiction of incorporation or organization	(I.R.S. Employer Identification No.)
3160 Porter Drive, Suite 250, Palo Alto, CA	**94304**
(Address of principal executive offices)	(Zip Code)

Registrant's telephone number, including area code: **(650) 391-9740**

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, par value $0.001 per share	BBIO	The Nasdaq Global Select Market

Securities registered pursuant to section 12(g) of the Act: **NONE**

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☒ No ☐

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes ☐ No ☒

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes ☒ No ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer	☒	Accelerated filer	☐
Non-accelerated filer	☐	Smaller reporting company	☐
		Emerging growth company	☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 726(b)) by the registered public accounting firm that prepared or issued its audit report. ☒

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements. ☐

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to §240.10D-1(b). ☐

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Act). Yes ☐ No ☒

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant based upon the closing price of the registrant's Common Stock on The Nasdaq Global Select Market on June 30, 2022 was approximately $976.8 million. Shares of the registrant's Common Stock held by each executive officer and director and by each other person who may be deemed an affiliate of the Registrant have been excluded from this computation. The determination of affiliate status for this purpose is not necessarily a conclusive determination for other purposes.

On February 16, 2023, there were 151,373,044 shares of the registrant's Common Stock issued and outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Specified portions of the registrant's definitive Proxy Statement to be issued in conjunction with the registrant's 2023 Annual Meeting of Stockholders, which is expected to be filed not later than 120 days after the registrant's fiscal year ended December 31, 2022, are incorporated by reference into Part III of this Annual Report. Except as expressly incorporated by reference, the registrant's Proxy Statement shall not be deemed to be a part of this Annual Report on Form 10-K.

BRIDGEBIO PHARMA, INC.
2022 Form 10-K Annual Report

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In this Annual Report on Form 10-K, unless otherwise stated or as the context requires, references to "BridgeBio," "the Company," "we," "us," "our" or similar references refer to BridgeBio Pharma, Inc., together with its consolidated subsidiaries.

Special Note Regarding Forward-Looking Statements

This Annual Report on Form 10-K contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. Such forward-looking statements involve substantial risks, uncertainties and assumptions. All statements in this Annual Report on Form 10-K, other than statements of historical fact, including, without limitation, statements regarding our strategy, future operations, future operating expenses, future financial position, future revenue, projected costs, prospects, plans, intentions, expectations, goals and objectives may be forward-looking statements. The words "anticipates," "believes," "could," "designed," "estimates," "expects," "goal," "intends," "may," "objective," "plans," "projects," "pursuing," "will," "would" and similar expressions (including the negatives thereof) are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. The forward-looking statements in this report include, but are not limited to, statements about:

- the success, cost and timing of our clinical development of our product candidates, including the progress of, and results from, our ongoing Phase 3 clinical trial of acoramidis, our ongoing Phase 2 and planned Phase 3 clinical trials of low-dose infigratinib, our ongoing Phase 2 and planned Phase 3 clinical trials of BBP-418, our ongoing Phase 1/2 clinical trial of BBP-631 and our ongoing Phase 2b and Phase 3 clinical trials of encaleret, as well as the potential indications for each;
- our ability to continue planned preclinical and clinical development of our respective development programs, and the timing, cost and success of any such continued preclinical and clinical development and planned regulatory submissions, including our KRAS inhibitor portfolio;
- our ability to initiate, recruit and enroll patients in and conduct our clinical trials at the pace that we project;
- the timing of our submissions to the U.S. Food and Drug Administration, or FDA, and any review or comments on data that we will need to generate to file our Investigational New Drug applications, or INDs, including pending or new clinical hold notices;
- our plans to implement certain development strategies, including our ability to attract and retain potential collaborators with development, regulatory and commercialization expertise;
- our ability to obtain and maintain regulatory approval of our product candidates in any of the indications for which we plan to develop them, and any related restrictions, limitations or warnings in the label of any of our product candidates, if approved;
- our ability to compete with companies currently marketing approved treatments or engaged in the development of treatments that may become available for any of the indications that our product candidates are designed to target;
- our reliance on third parties to conduct our clinical trials and to manufacture drug substance for use in our clinical trials;
- our ability to contract with and the performance of our and our collaborators' third-party suppliers and manufacturers;
- the pricing and reimbursement of our product candidates, if approved;
- the size and growth potential of the markets for our product candidates, including acoramidis, low-dose infigratinib, BBP-418, BBP-631, encaleret, any KRAS inhibitor candidates, and any of our current product candidates or other product candidates we may identify and pursue, and our ability to serve and our acceptance by those markets;
- our ability to identify and advance through clinical development any additional product candidates, including in our KRAS inhibitor portfolio for the treatment of KRAS-driven cancers;
- the commercialization of our current product candidates, if approved, and any other product candidates we may identify and pursue, if approved, including our ability to successfully build a specialty sales force and commercial infrastructure to market our current product candidates and any other product candidates we may identify and pursue;

- the implementation and effects of the restructuring initiative that we commenced in January 2022 and any future restructuring plans that we may pursue;
- the impacts of the ongoing COVID-19 pandemic and macroeconomic factors that could impact our business, such as the effects of the Russian invasion of Ukraine on the global economy and supply chain and inflationary pressures;
- our ability to retain and recruit key scientific or management personnel;
- the success of competing therapies that are or may become available;
- our ability to obtain and maintain adequate intellectual property rights for our product candidates and our ability to operate our business without infringing on the intellectual property rights of others;
- our expectations regarding government and third-party payor coverage and reimbursement;
- our estimates of our expenses, ongoing losses, capital requirements and our use of cash resources, and our needs for or ability to pay for debt interests and obtain additional financing to complete the clinical trials of any of our product candidates;
- the impact of laws and regulations in the United States and foreign countries;
- our financial performance; and
- developments and projections relating to our competitors or our industry.

We may not actually achieve the plans, intentions, expectations or objectives disclosed in our forward-looking statements and the assumptions underlying our forward-looking statements may prove incorrect. Furthermore, if our forward-looking statements prove to be inaccurate, the inaccuracy may be material. Therefore, you should not place undue reliance on our forward-looking statements, and you should not regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified time frame, or at all. Actual results or events could differ materially from the plans, intentions, expectations and objectives disclosed in the forward-looking statements that we make. Important factors that we believe could cause actual results or events to differ materially from our forward-looking statements include, but are not limited to, those listed under “Risk Factors” in Item 1A of Part I, “Management’s Discussion and Analysis of Financial Condition and Results of Operations” in Item 7 of Part II and elsewhere in this Annual Report on Form 10-K. Our forward-looking statements in this Annual Report on Form 10-K are based on current expectations as of the date hereof and we do not assume any obligation to update any forward-looking statements on account of new information, future events or otherwise, except as required by law.

RISK FACTOR SUMMARY

Below is a summary of the principal factors that make an investment in our common stock speculative or risky. This summary does not address all of the risks that we face. Additional discussion of the risks summarized in this risk factor summary, and other risks that we face, can be found below under the heading "Risk Factors" and should be carefully considered, together with other information in this Annual Report on Form 10-K and our other filings with the U.S. Securities and Exchange Commission, or the SEC, before making investment decisions regarding our common stock.

- Certain of our product candidates are in preclinical or clinical development, which is a lengthy and expensive process with uncertain outcomes and the potential for substantial delays. We may not receive regulatory approval to market any of these product candidates in any jurisdictions, which would materially and adversely affect our business, prospects, operating results and financial condition.
- Our clinical trials may fail to demonstrate substantial evidence of the safety and efficacy of product candidates that we may identify and pursue for their intended uses, which would prevent, delay or limit the scope of regulatory approval and commercialization.
- Drug development is a highly uncertain undertaking and involves a substantial degree of risk. We have incurred significant losses since our inception and anticipate that we will continue to incur significant losses for the foreseeable future. We have not generated significant product revenue since inception, which, together with our limited operating history, may make it difficult for you to assess our future viability.
- We may encounter substantial delays in clinical trials for a variety of reasons, including difficulties in patient enrollment, and we may not be able to conduct or complete clinical trials on the expected timelines, if at all.
- Results of earlier studies or clinical trials may not be predictive of future clinical trial results, and initial studies or clinical trials may not establish an adequate safety or efficacy profile for our product candidates to justify proceeding to advanced clinical trials or an application for regulatory approval.
- Use of our product candidates could be associated with side effects, adverse events or other properties or safety risks, which could delay or halt their clinical development, prevent their regulatory approval, cause us to abandon a product candidate, limit their commercial potential, if approved, or result in other significant negative consequences to our business, prospects, operating results and financial condition.
- Certain of our product candidates are under development for the treatment of patient populations with significant comorbidities that may result in deaths or serious adverse or unacceptable side effects and require us to abandon or limit our clinical development activities.
- Interim, "top-line," and preliminary data from our clinical trials that we announce or publish from time to time may not be predictive of future clinical trial results and may change as more data become available, as additional analyses are conducted, or as audit and verification procedures are performed on such preliminary data.
- Our conduct of clinical trials for product candidates and our plans to commercialize certain product candidates outside the United States could expose us to additional risks and uncertainties, including with respect to our ability to obtain regulatory approvals or comply with applicable laws and regulations outside the United States.
- Even though we may apply for orphan drug designation for our product candidates, we may not be able to obtain orphan drug marketing exclusivity.
- Even if we obtain regulatory approval for any of our current product candidates, we will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant expense to maintain compliance with such obligations or as a result of any penalties to which we may become subject for any failure to comply with such obligations.
- Certain of our product candidates, including our protein therapeutic and gene therapy product candidates, are novel, complex and difficult to manufacture. We could experience manufacturing problems that delay our development or commercialization activities or otherwise harm our business.

- Certain of our product candidates are based on a novel adeno-associated virus, or AAV, gene therapy technology with which there is limited clinical or regulatory experience to date, which makes it difficult to predict the time and cost of product candidate development and subsequently obtaining regulatory approval.
- We face significant competition from other biotechnology and pharmaceutical companies, and our operating results will suffer if we fail to compete effectively.
- Our future success depends on our ability to retain key employees, directors, consultants and advisors and to attract, retain and motivate qualified personnel.
- We will need substantial additional financing to develop and, if approved, commercialize our product candidates and implement our operating plans. If we fail to obtain additional financing, when needed on acceptable terms, or at all, we may be forced to delay, reduce or terminate our research and development programs, future commercialization efforts or other operations.
- We rely and will continue to rely on third parties to conduct our clinical trials and some aspects of our research and preclinical testing, and for the manufacture of our product candidates for preclinical studies and clinical trials and, if approved, any products that we determine to commercialize. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, we may not be able to obtain regulatory approval of or commercialize our product candidates.
- Our rights to develop and commercialize our product candidates are subject in part to the terms and conditions of licenses granted to us by others, and the patent protection, prosecution and enforcement for some of our product candidates may be dependent on our licensors, the loss of which could result in the loss of intellectual property and other protection, and would harm our business.
- If we are unable to obtain and maintain sufficient intellectual property protection for our product candidates, including acoramidis, low-dose infigratinib, BBP-418, BBP-631 encaleret, and our KRAS inhibitor portfolio, or if the scope of the intellectual property protection obtained is not sufficiently broad, our competitors could develop and commercialize products or product candidates similar or identical to ours, and our ability to successfully commercialize our potential product candidates may be impaired.
- If any of our current product candidates receive marketing approval, they may fail to achieve the degree of market acceptance by physicians, patients, healthcare payors, and others in the medical community necessary for commercial success.
- Because we have multiple programs and product candidates in our development pipeline and are pursuing a variety of target indications and treatment modalities, we may expend our limited resources to pursue a particular product candidate and fail to capitalize on development opportunities or product candidates that may be more profitable or for which there is a greater likelihood of success.
- We have incurred a significant amount of debt and may in the future incur additional indebtedness. Servicing our debt requires a significant amount of cash, and we may not have sufficient cash flow from our business to pay our substantial debt.
- The ongoing COVID-19 pandemic, including newly discovered variants, could adversely impact our business, including our clinical trials and preclinical studies.
- Unfavorable global economic conditions, including market volatility, inflationary pressures, acts of war and civil and political unrest, could have a negative impact on our stock price, increase our operating expenses and impair our ability to raise additional capital on acceptable terms, or at all.

PART I

ITEM 1. BUSINESS

Overview

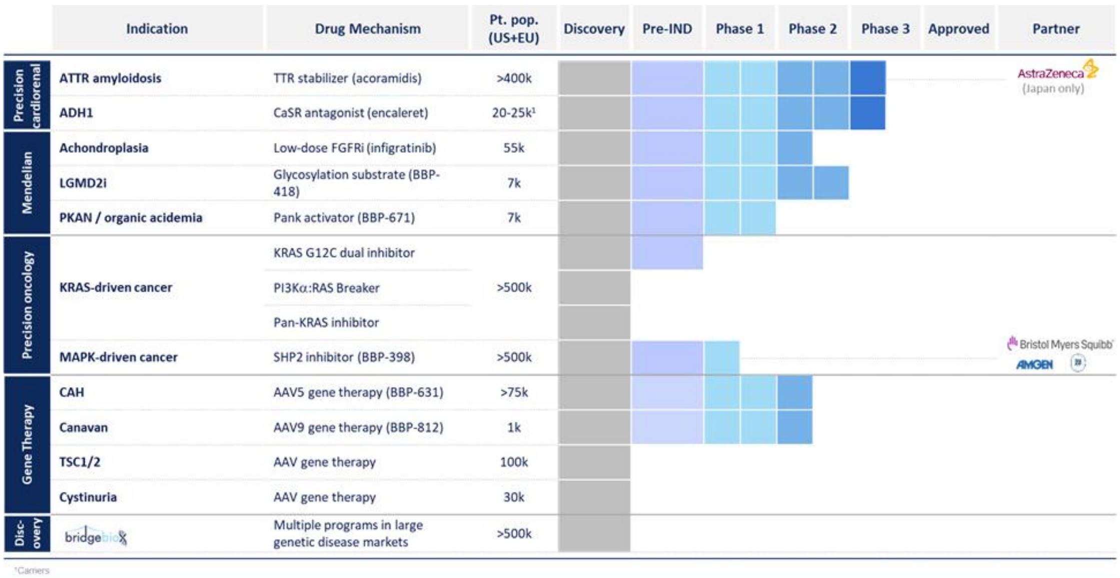
BridgeBio Pharma, Inc. is a commercial-stage biopharmaceutical company founded to discover, create, test and deliver transformative medicines to treat patients who suffer from genetic diseases and cancers with clear genetic drivers. BridgeBio's pipeline of development programs ranges from early science to advanced clinical trials. BridgeBio was founded in 2015 and its team of experienced drug discoverers, developers and innovators are committed to applying advances in genetic medicine to help patients as quickly as possible. Since inception, BridgeBio has created 15 Investigational New Drug applications, or INDs, and had two products approved by the U.S. Food and Drug Administration. We work across over 20 disease states at various stages of development. Several of our programs target indications that we believe present the potential for our product candidates, if approved, to target portions of market opportunities of at least $1.0 billion in annual sales.

We focus on genetic diseases because they exist at the intersection of high unmet patient need and tractable biology. Our approach is to translate research pioneered at academic laboratories and leading medical institutions into products that we hope will ultimately reach patients. We are able to realize this opportunity through a confluence of scientific advances, including: (i) identification of the genetic underpinnings of disease as more cost-efficient genome and exome sequencing becomes available; (ii) progress in molecular biology; and (iii) the development and maturation of longitudinal data and retrospective studies that enable the linkage of genes to diseases. We believe that this early-stage innovation represents one of the greatest practical sources for new drug creation.

We believe we have developed a world-class product platform that supports the continued growth of our Company and the advancement of our pipeline.

Our Pipeline

Our pipeline could deliver up to eight potential Phase 3 readouts over the next five years, of which we expect acoramidis, low-dose infigraitinib, encaleret, BBP-418 and BBP-631 to be in markets of one billion dollars or more. The following table summarizes our development programs, their estimated patient populations, their therapeutic modalities and their development status:



Of our investigational programs, we believe the following have the greatest potential to drive significant near-term value for our Company due to a combination of factors, including their stage of development, potential availability of expedited development pathways, degree of unmet medical need and potential market size in the applicable target indication:

- Acoramidis (also known as AG10), a small molecule stabilizer of transthyretin, or TTR, that is in an ongoing Phase 3 clinical trial for the treatment of TTR amyloid cardiomyopathy, or ATTR-CM.
- Low-dose infigratinib, a small molecule selective FGFR1-3 inhibitor that is in an ongoing Phase 2 clinical trial for the treatment of children with achondroplasia.
- Encaleret, a small molecule antagonist of the calcium sensing receptor, or CaSR, that is in ongoing Phase 2b and Phase 3 pivotal clinical trials for Autosomal Dominant Hypocalcemia Type 1, or ADH1.
- BBP-418, an orally administered substrate replacement product candidate that has delivered positive interim data from an ongoing Phase 2 clinical trial for the treatment of Limb-Girdle Muscular Dystrophy type 2I, or LGMD2I, with a Phase 3 clinical trial planned to start in 2023.
- BBP-631, an AAV5 gene transfer product candidate that is in an ongoing Phase 1/2 clinical trial for the treatment of congenital adrenal hyperplasia, or CAH, driven by 21-hydroxylase deficiency, or 21OHD.
- KRAS inhibitor portfolio for the treatment of KRAS-driven cancers, including:
  - BBO-8520, a next-generation KRAS G12C dual GTP/GDP inhibitor, which has shown greater potency in preclinical KRAS models than first-generation KRAS G12C GDP-only inhibitors and which we plan to enter into the clinic in 2023;
  - a novel PI3Kα:RAS breaker molecule, which we intend to move into IND-enabling studies in 2023; and
  - a preclinical pan-KRAS inhibitor program in lead optimization.

Acoramidis (Eidos): TTR Amyloidosis

Summary

We are developing acoramidis, also known as AG10, an oral small molecule TTR stabilizer, for the treatment of TTR amyloidosis, or ATTR. A Phase 3 clinical trial in 632 patients with ATTR cardiomyopathy, or ATTR-CM, known as the ATTRibute-CM study, is currently ongoing. We anticipate reporting top-line 30-month outcomes data from Part B of the ATTRibute-CM study in mid-2023. We continue to believe acoramidis has the potential to demonstrate benefit on the 30-month hierarchical composite primary endpoint, which includes all-cause mortality and cardiovascular-related hospitalizations.

On December 27, 2021, we reported that ATTRibute-CM did not meet its Part A primary endpoint of change for baseline in six-minute walk distance at Month 12. We observed improvements in acoramidis-treated participants relative to placebo-treated participants at Month 12 on key secondary and exploratory endpoints including on N-terminal pro BNP, or NT-proBNP, a cardiac biomarker, and serum TTR concentration, a measure of TTR stabilization and the Kansas City Cardiomyopathy Questionnaire Overall Score, or KCCQ-OS, a quality-of-life measurement.

Market Opportunity

We believe that the total market for ATTR therapeutic interventions will continue to grow for the foreseeable future as the population of diagnosed patients increases as a result of heightened disease awareness and the increased adoption of non-invasive diagnostic techniques. The number of estimated diagnosed ATTR-CM patients in the United States has grown from fewer than 5,000 in 2019 to more than 30,000 in 2021. As such, if acoramidis is approved, we believe that there could be a significant population of newly diagnosed patients who have not previously been treated with a disease-modifying therapy and could be treated with acoramidis. If approved, we believe that acoramidis could have meaningful commercial potential. Further, we believe that acoramidis, if approved, has the potential to be a best-in-class stabilizer for the treatment of ATTR.

Disease Overview

ATTR is a disease caused by destabilization of TTR tetramers resulting in progressive amyloid deposition. TTR is a protein that occurs naturally in the form of a tetramer, consisting of four identical subunits, or monomers, and performs multiple physiologic roles, including the transport of essential hormones and vitamins. In ATTR, TTR tetramers become destabilized due to a mutation in the *TTR* gene or as part of the natural aging process. Destabilized TTR dissociates into monomers, self-aggregates, and assembles into fibrils that are deposited, predominantly in the heart and nervous system, driving disease pathophysiology.

Cardiomyopathic ATTR is commonly categorized by its genotypic cause with wild-type ATTR cardiomyopathy, or ATTRwt-CM, which results from an age-related process, and variant ATTR cardiomyopathy, or ATTRv-CM. Both forms of the disease are progressive and fatal. ATTRwt-CM and ATTRv-CM patients generally present with symptoms later in life (older than 50) and have median life expectancies of two to five years from diagnosis if untreated. Progression of both forms of the disease can cause significant disability, impact productivity and quality of life, and create a significant economic burden due to the costs associated with patient need for supportive care. As the disease progresses, ATTRwt-CM and ATTRv-CM patients may experience recurrent hospitalizations and repeated interventions.

The worldwide estimated prevalence of ATTRwt-CM and ATTRv-CM is greater than 400,000 and 40,000, respectively. We believe that cardiomyopathic ATTR is significantly underdiagnosed today. For example, recent literature has suggested that between 10% to 13% of patients diagnosed with heart failure with preserved ejection fraction may have undiagnosed ATTR-CM. The heart failure with preserved ejection fraction segment represents approximately half of the 6.0 million to 7.0 million estimated people with heart failure in the United States. With the increasing availability of disease-modifying therapeutics, disease awareness is heightened.

We believe the population of diagnosed ATTR-CM patients is also growing rapidly due to the shift to an accurate and reliable non-invasive diagnostic imaging technique. Historically, a heart biopsy was required to make a diagnosis of ATTR-CM. Recently, however, it has been shown that scintigraphy with technetium-labelled radiotracers paired with single-photon emission computerized tomography, or SPECT, CT imaging is a highly accurate, non-invasive, and cost-effective method for ATTR-CM diagnosis. We believe that both increased disease awareness and availability of this non-invasive diagnostic imaging technique are allowing for earlier diagnosis of ATTR-CM patients and the identification of previously misdiagnosed patients.

Design Criteria

Acoramidis is a clinical-stage, orally administered, small molecule TTR stabilizer being developed to treat ATTR at its source. We designed acoramidis to meet two primary criteria – to preserve circulating native TTR and to reduce amyloid deposition by minimizing toxic TTR monomer formation.

TTR is a protein which has been highly conserved throughout evolution, and which is abundant in the plasma with relatively rapid turnover requiring sustained metabolic energy expenditure. Thus, we seek to achieve maximal stabilization of the TTR tetramer rather than elimination.

Acoramidis has been shown in preclinical studies and clinical trials to prevent the dissociation of tetrameric TTR into monomers, and in preclinical studies, to reduce the rate of amyloid fibril formation. In addition, it has been shown to lead to increased circulating levels of tetrameric TTR. Acoramidis has been designed to bind TTR in a way that causes TTR's conformational structure to mimic that of the well-characterized T119M variant, a naturally occurring rescue mutation that super stabilizes the TTR tetramer. The T119M variant has been observed to prevent the dissociation of TTR tetramers into monomers; T119M tetramers dissociate 40-fold more slowly than wild-type tetramers in biochemical assays. Known as a trans-allelic trans-suppressor, individuals who coinherit the T119M rescue mutation along with a TTR-destabilizing mutation are protected against the development of ATTR.

In third-party clinical trials of tafamidis, another orally administered, small molecule TTR stabilizer, interventional approaches that increased TTR stabilization led to improved outcomes in this disease, as measured by all-cause mortality and cardiovascular-related hospitalizations, and were correlated with increases in serum TTR. Further, based on genetic data, there is a correlation between the level of TTR stabilization, serum TTR levels and disease severity. As a result, we believe that serum TTR is a predictive biomarker for disease prognosis and that there may be a relationship between more effective TTR stabilization, serum TTR levels and improved clinical outcomes. Based on results from comparative nonclinical studies, we believe that acoramidis has the potential to stabilize TTR to a greater extent than other TTR stabilizers.

Clinical Data

Phase 2 Data

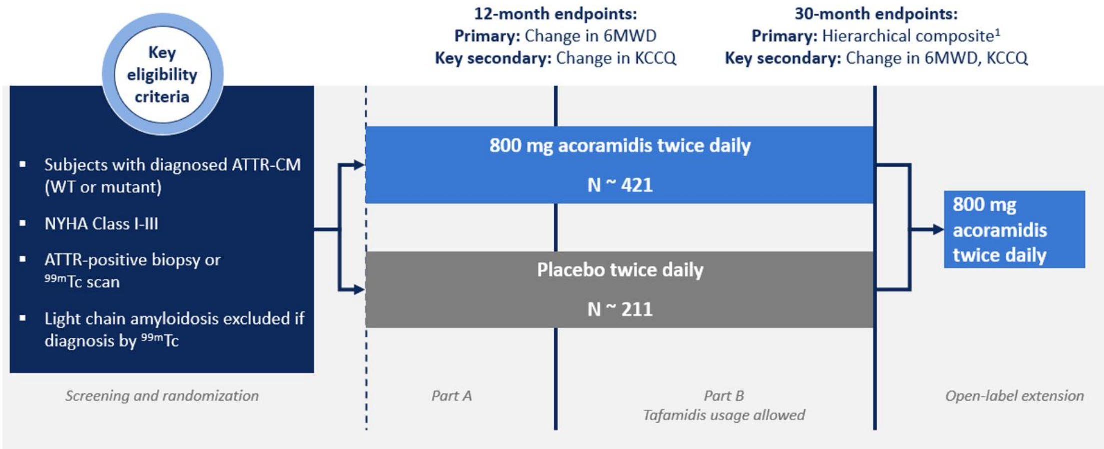
In November 2018, we announced Phase 2 data for acoramidis in symptomatic patients with ATTR-CM. The randomized, placebo-controlled, dose-ranging clinical trial included 49 patients with symptomatic ATTR-CM, of which 14 had ATTR-CM. Eligible patients were randomized in a 1:1:1 ratio to placebo or 400 milligrams or mg, or 800 mg of acoramidis twice daily over 28 days. Overall, acoramidis was well-tolerated in symptomatic ATTR-CM subjects with no safety signals of potential clinical concern attributed to study drug. Acoramidis significantly raised serum TTR concentrations ($p < 0.0001$) by 50% and 36% in subjects administered 800 mg twice daily and 400 twice daily, respectively, at day 28. Normalized serum TTR levels were observed in all actively treated subjects at day 28.

In November 2019, we announced data from our Phase 2 open-label extension, or OLE, suggesting long-term tolerability of acoramidis and stabilization of ATTR-CM disease measures. Acoramidis was well-tolerated in the OLE and no safety signals of potential clinical concern were attributed to study drug. The rate of all-cause mortality (including either death or cardiac transplantation, 8.5%) and cardiovascular-related hospitalizations (proportion experiencing at least one event, 25.5%) observed in an exploratory analysis of OLE participants following a median of 15 months since Phase 2 initiation were lower than those observed at 15 months in placebo-treated patients in the ATTR-ACT study (all-cause mortality including death or cardiac transplantation, 15.3%; cardiovascular-related hospitalizations, 41.8%).

In April 2022, we presented updated results from our Phase 2 OLE, demonstrating continued long-term tolerability of acoramidis and stabilization of ATTR-CM disease measures. With a median of 38 months of continuous treatment, acoramidis was generally well-tolerated in the OLE and no safety signals of potential clinical concern were attributed to study drug.

Phase 3 Data

In February 2019, we initiated ATTRibute-CM, a global Phase 3 randomized, placebo-controlled clinical trial of acoramidis in ATTR-CM. ATTRibute-CM enrolled 632 subjects with symptomatic ATTR-CM, associated with either wild-type or variant TTR and New York Heart Association, or NYHA, Class I-III symptoms. Subjects were randomized 2:1 between treatment (acoramidis 800 mg) and placebo twice daily in a two-part trial. In Part A, change in 6MWD at 12 months was compared between treatment and placebo groups as a potential registrational endpoint. In Part B, the hierarchical composite primary endpoint including all-cause mortality and cardiovascular hospitalizations will be compared between treatment and control groups at 30 months. Secondary endpoints include quality of life as assessed by the KCCQ-OS, safety parameters, serum TTR levels, a measure of TTR stabilization, and NT-proBNP levels, a cardiac biomarker. In Part B, concomitant use of tafamidis is allowed. A schematic of the trial is shown below:



6MWD = Six-minute walk distance KCCQ = Kansas City Cardiomyopathy Questionnaire NYHA = New York Heart Association
^{99m}Tc = Technetium labeled pyrophosphate (PYP) or bisphosphonate (e.g., DPD) CV = cardiovascular-related
[1]Primary analysis will use the Finkelstein-Schoenfeld method

On December 27, 2021, we reported topline data from Part A of the ATTRibute-CM trial which did not meet its primary endpoint of change from baseline in 6MWD (p = 0.76). Mean observed 6MWD decline for the acoramidis and placebo arms were 9 meters and 7 meters, respectively. Decline observed in both arms of ATTRibute-CM was similar to expected functional decline in healthy elderly adults at 12 months. We observed improvements in acoramidis-treated participants relative to placebo-treated participants at Month 12 on secondary and exploratory endpoints including NT-proBNP, serum TTR concentration and KCCQ-OS.

Acoramidis was generally well-tolerated with no safety signals of clinical concern identified. To protect the integrity of Part B, as sponsor, our access to unblinded adverse event data for Part A excludes adverse events leading to a cardiovascular hospitalization (as determined by investigators) excepting events with the outcome of death. Adverse events, or AEs, occurred in 85.3% of placebo-treated participants and 91.9% of acoramidis-treated participants. In both the placebo and active treatment groups, most of the AEs were mild to moderate in severity. Serious adverse events, or SAEs, occurred in 23.2% of placebo-treated participants and 20.2% of acoramidis-treated participants. AEs leading to death occurred in 6.2% of placebo-treated participants and 4.5% of acoramidis-treated participants.

We continue to believe acoramidis has the potential to demonstrate benefit on the 30-month hierarchical composite primary endpoint, which includes all-cause mortality and cardiovascular-related hospitalizations. We anticipate reporting top-line 30-month results from Part B of the ATTRibute-CM trial in mid-2023.

Competition

If acoramidis is approved as a treatment for ATTR-CM, we expect to face competition from Vyndaqel / Vyndamax (tafamidis meglumine / tafamidis), which is approved in certain territories, including the United States, the European Union, and Japan as a treatment for ATTR-CM. Additionally, there are a number of RNAi, antisense oligonucleotide, antibody, and gene editing product candidates that are currently in development as potential treatments for ATTR-CM.

Low-dose Infigratinib: Achondroplasia

Summary

We are developing low-dose infigratinib, an oral FGFR1-3 selective tyrosine kinase inhibitor, or TKI, as a treatment option for children with achondroplasia. We are currently enrolling patients in PROPEL, a prospective observational study in children with achondroplasia and PROPEL 2, a Phase 2 dose-escalation and expansion study of low-dose infigratinib in children with achondroplasia. In July 2022, we reported initial data showing an increase from baseline in annualized growth velocity of +1.52 cm per year in children with achondroplasia ages 5 or older in PROPEL2's fourth dose escalation cohort (0.125 mg/kg once a day). We have enrolled a fifth dose (0.25 mg/kg once a day) escalation cohort and anticipate sharing preliminary early results in the first quarter of 2023.

Market Opportunity

We believe that achondroplasia and other FGFR-driven skeletal dysplasias represent a potentially over five billion dollar total global market opportunity. The achondroplasia market alone has grown steadily since the end of 2021, driven by a newly available therapy driving children to seek treatment, as well as growing awareness of the new treatment among pediatric endocrinologists. We believe that low-dose infigratinib, if approved, would have meaningful commercial potential to demonstrate best-in-class efficacy as well as a differentiated oral route of administration preferred by many patients.

Condition Overview

Achondroplasia is the most frequent cause of disproportionate short stature, and mutations in the FGFR3 gene have been shown to be the molecular source of the condition. Achondroplasia has a prevalence of greater than 55,000 in the United States and European Union, and an estimated worldwide incidence of one in 10,000 to 30,000 live births. The condition leads to a disproportionate short stature with anomalies in bone development and potential for foramen magnum stenosis, spinal stenosis, cardiovascular complications and obesity. The average height is approximately 4'4" for a male and 4'1" for a female with achondroplasia. Lifespan and intelligence are most often normal.

Achondroplasia is an autosomal dominant condition caused by a gain-of-function point mutation in the FGFR3 gene. Approximately 97% of cases are due to G380R substitution and 80% of cases are the result of *de novo* mutations. FGFR3 is expressed in osteoblasts and chondrocytes where it plays a critical role in regulating bone growth through the MAPK pathway, which drives hypertrophic differentiation, and through the STAT1 pathway, which drives chondrocyte proliferation. Apart from growth hormones, which are approved in Japan, there is only one medicine approved for marketing by the FDA, European Medicines Agency, or the EMA, and the Pharmaceuticals and Medical Devices Agency, or PMDA, for the treatment of achondroplasia: Voxzogo (vosoritide), a C-type natriuretic peptide, or CNP, analog which activates the MAPK pathway but not the STAT1 pathway.

Design Criteria

We are developing low-dose infigratinib based upon two key design principles – we seek to target achondroplasia at its source (FGFR3 gain-of-function mutations) in order to maximize clinical activity against all manifestations of the condition, not just height; and we seek to provide a tolerable oral treatment option in order to provide a reduced burden of treatment versus injection for children and their families. We believe low-dose infigratinib is the only investigational therapy in development that incorporates both of these design principles.

Low-dose infigratinib is designed to directly target FGFR3 gain-of-function mutations which are the drivers behind the pathophysiology of achondroplasia. As an FGFR1-3 inhibitor, we believe that low-dose infigratinib has the potential to decrease pathologic signaling downstream of FGFR3 and treat achondroplasia at its source. Unlike potentially competitive CNP mimetic approaches, which only inhibit MAPK signaling, our approach is aimed at also inhibiting STAT1 signaling.

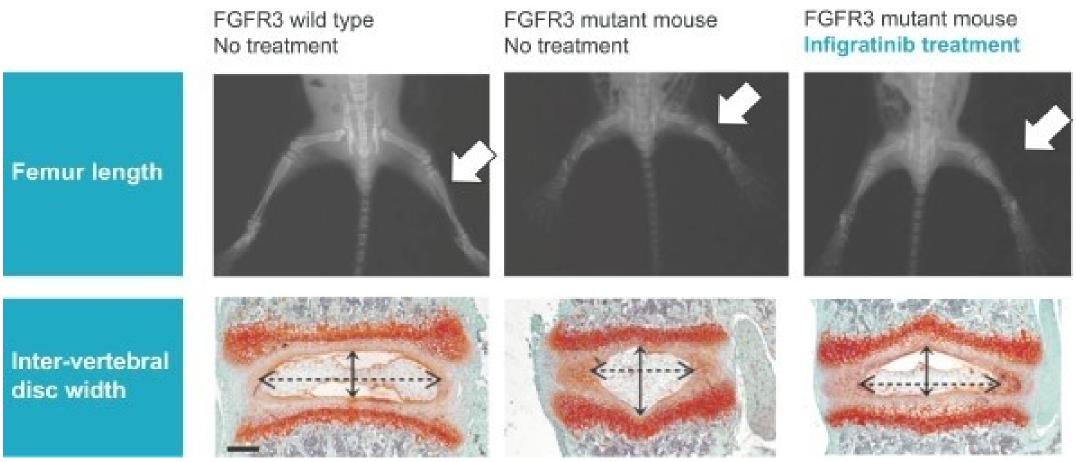
Low-dose infigratinib is also designed for an oral route of administration. Blinded market research indicates that oral administration is the preferred route of administration amongst healthcare providers who treat children with achondroplasia.

In the four dosing cohorts completed in our Phase 2 dose escalation trial as well as in the fifth dosing cohort as of February 9, 2023, low-dose infigratinib has been generally well-tolerated with no serious adverse events reported. As of February 9, 2023, there have been no discontinuations due to adverse events, no dose-dependent phosphate elevation, and no ocular adverse events.

Preclinical Data

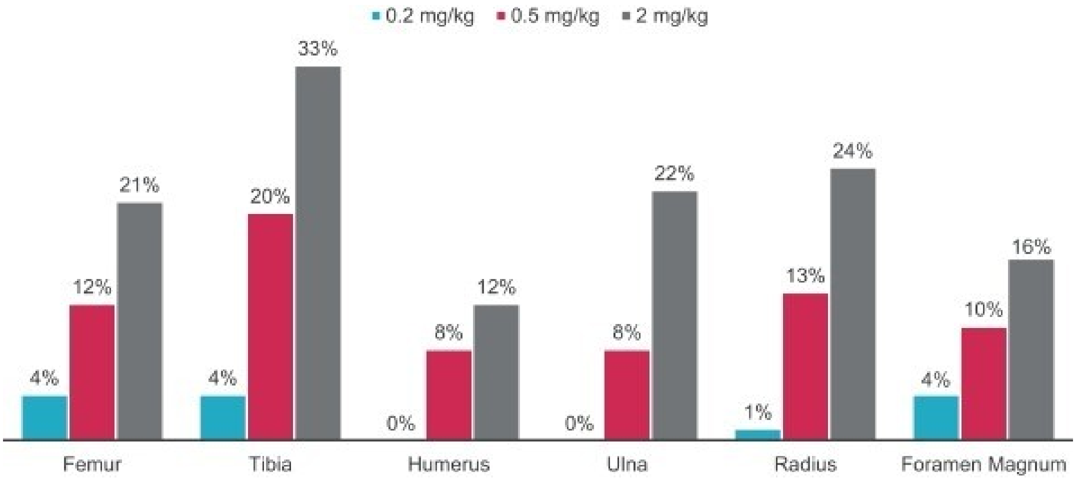
Low-dose infigratinib has been studied preclinically in a mouse model of achondroplasia that recapitulates anomalies of the growth plates, vertebrae, and intervertebral discs. Investigators observed that low-dose infigratinib rescued *ex vivo* bone growth of mutant mouse embryo femurs after six days of treatment. Further, 15 days of treatment showed *in vivo* bone growth, which mimics human achondroplasia in many respects. Effects on both appendicular and axial skeletal parameters were observed in this study.

Below are figures demonstrating the extent of femur growth and intervertebral disc width rescue in wild-type, untreated model, and low-dose infigratinib treated (2 mg/kg) model mice:



In vivo bone growth was further demonstrated at lower doses (0.2 mg/kg and 0.5 mg/kg) by the same laboratory. Together, preclinical studies at all doses have demonstrated meaningful increases in skeletal growth parameters between treated and untreated mutant mice, as follows:

Increase in length compared to non-treated mouse (%)



Notably, treatment with low-dose infigratinib did not modify the expression of FGFR1 in the hypertrophic zone of the growth plate. The effects seen were mainly due to FGFR3 inhibition, with no other gross side effects being observed in these preclinical studies. Furthermore, survival was improved after 15 days in low-dose infigratinib treated mice, regardless of dose, as compared to untreated mice.

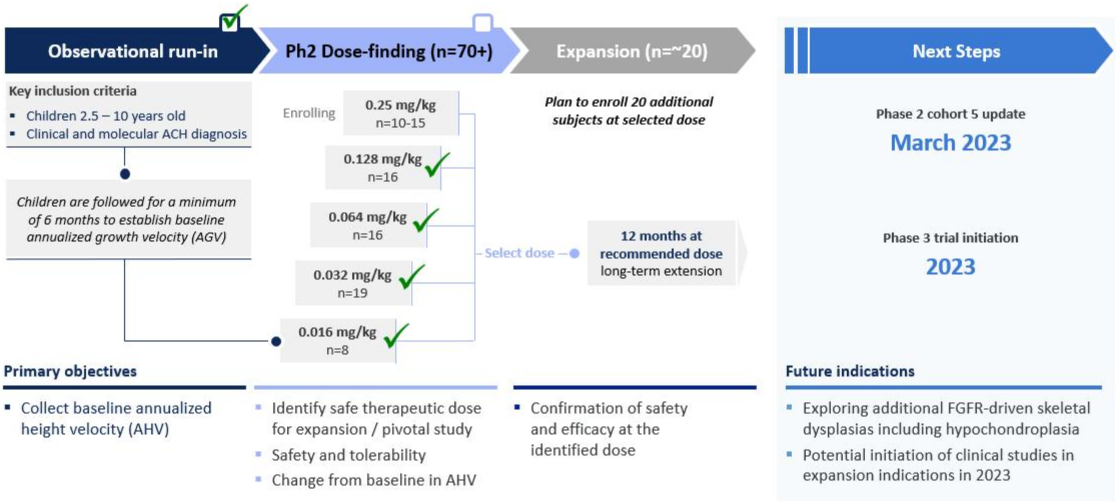
Clinical Development Plan

We are currently enrolling patients in PROPEL, a prospective observational study in children with achondroplasia. The study will establish annualized growth velocity, or AGV, for each child for a minimum period of six months. PROPEL is designed to provide baseline measurements for children that we anticipate enrolling in either PROPEL 2, an ongoing Phase 2 study of low-dose infigratinib, or in an anticipated Phase 3 trial to follow.

PROPEL 2 is designed as an open-label, dose-escalation and expansion trial in children with achondroplasia prior to growth plate closure. The primary objective of this study is to assess safety and tolerability in children with achondroplasia. Secondary objectives will include PK analyses, change in growth velocity, and assessment of quality of life.

In July 2022, we reported initial data showing an increase from baseline in annualized growth velocity of +1.52 cm per year in children with achondroplasia ages 5 or older in PROPEL2’s fourth dose escalation cohort. We have enrolled a fifth dose escalation cohort and anticipate sharing preliminary early results in the first quarter of 2023.

We anticipate initiating a Phase 3 pivotal trial for low-dose infigratinib in achondroplasia in 2023, following feedback from the FDA.



Key Competitors

Low-dose infigratinib is the only oral direct FGFR1-3 inhibitor that has been publicly disclosed in development for the treatment of achondroplasia. There are three other identified companies developing compounds for the treatment of achondroplasia using alternative mechanistic approaches: Ascendis Pharma A/S (TransCon CNP), Sanofi S.A. (SAR442501), and Ribomic (RBM-007). In addition, BioMarin Pharmaceutical Inc. has developed Voxzogo (vosoritide), a CNP analog, for the treatment of achondroplasia.

Encaleret: Autosomal Dominant Hypocalcemia Type 1 and Hypoparathyroidism

Summary

Encaleret is an oral small molecule antagonist of the calcium sensing receptor, or CaSR, that we are developing for the treatment of Autosomal Dominant Hypocalcemia Type 1, or ADH1. We are currently studying encaleret in ongoing Phase 2b and Phase 3 clinical trials as a potential treatment for patients with ADH1. We reported results from the Phase 2b study in 2022. In 13 participants in the Phase 2b trial, treatment with encaleret resulted in rapid and sustained restoration of normal mineral homeostasis, with mean values of blood calcium, urinary calcium, and blood parathyroid hormone, or PTH within the normal range by day 5 of therapy and sustained at 24 weeks, and was well-tolerated without any reported serious adverse events. Encaleret has been granted orphan drug and fast track designations by the FDA for the treatment of autosomal dominant hypocalcemia. Encaleret has also been granted orphan designation by the European Commission as a treatment for hypoparathyroidism, inclusive of ADH1.

Market Opportunity

We believe that ADH1 is a market with significant commercial potential. ADH1 is caused by gain-of-function variants of the CASR gene, and independent studies of general population genetic datasets estimate that there are 25,000 carriers of ADH1-causative variants in the EU and US. If approved, encaleret could be the first target-directed therapy indicated for ADH1.

Design Criteria

Encaleret is an investigational, orally administered, small molecule antagonist of the CaSR. It has been studied in more than 1,200 human subjects in its prior development and was observed to increase serum calcium in a dose-dependent manner. The rationale for developing encaleret as a potential treatment for patients with ADH1 is based on both non-clinical and clinical evidence. Antagonists of the CaSR have been shown *in vitro* to shift the aberrant CaSR "set-point" back towards a normal IC_{50} for calcium and *in vivo* to increase PTH secretion, elevate blood calcium concentrations, and reduce urinary calcium excretion. By selectively antagonizing the CaSR, encaleret may restore normal CaSR function in individuals with ADH1 and may address symptoms associated with hypocalcemia and hypercalciuria

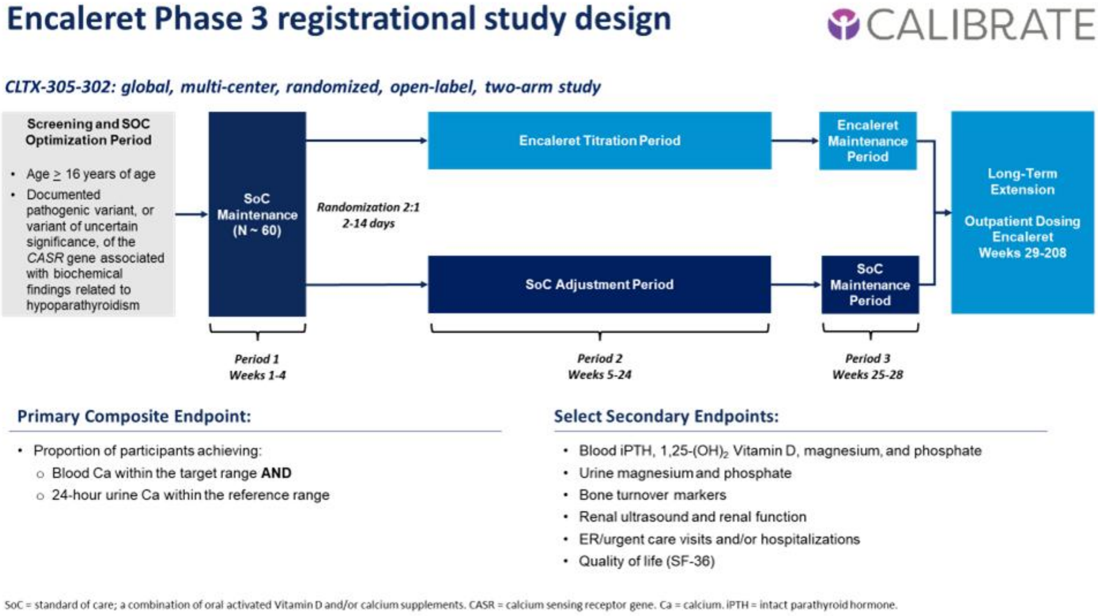
Clinical Data

On June 13, 2022, we reported positive data from our Phase 2b clinical trial of encaleret in patients with ADH1. Thirteen adults with ADH1 caused by nine unique *CASR* variants participated in the three-period, Phase 2b, open-label, dose-ranging clinical trial. Oral calcium and activated vitamin D supplements were discontinued prior to encaleret initiation. Periods 1 and 2 each evaluated encaleret over the course of five inpatient days and Period 3 included a 24-week outpatient evaluation. Based on 24-week outpatient data, we observed:

- Mean values of blood calcium, urinary calcium, and blood parathyroid hormone, key biochemical parameters of mineral homeostasis, were normalized by Period 2, Day 5 and were sustained through Period 3, Week 24 of the trial.
- At Week 24 of encaleret treatment, 92% (12/13) of participants had achieved normal trough blood calcium levels in the absence of extra-dietary calcium supplements and active vitamin D, and 77% (10/13) of participants had normal urinary calcium excretion.
- Encaleret was well-tolerated with no serious adverse events reported; there were no treatment discontinuations or study withdrawals.

The participants who completed Period 3 of the study were eligible to continue in an open-label extension of up to 25 months.

We also announced the initiation of our Phase 3 registrational trial of encaleret in ADH1 in 2022.



Key Competitors

We believe encaleret is the only molecule that has been publicly disclosed to be in development specifically for the treatment of ADH1. There are other identified companies developing compounds for the treatment of hypoparathyroidism using recombinant parathyroid hormone analogs or PTH receptor agonists: Ascendis Pharma A/S (TransCon PTH), Amolyt Pharma (AZP-3601), EnteraBio Ltd. (EB612), and Extend Biosciences Inc. (EXT607).

BBP-418: Limb Girdle Muscular Dystrophy Type 2I

BBP-418 is an investigational, orally administered, small molecule substrate replacement therapy that we are developing for the treatment of LGMD2I, also known as LGMDR9. We are currently studying BBP-418 in an ongoing open-label dose-ascending Phase 2 clinical trial in patients with LGMD2I. We reported top-line data in October 2022. We anticipate initiating a global Phase 3 clinical trial in 2023.

Disease Overview

LGMD2I is an inherited neuromuscular disorder characterized by lower-limb weakness and loss of ambulation, and possible pulmonary and cardiac dysfunction. BBP-418 has a potentially-addressable population of 7,000, including both LGMD2I and other potentially-addressable dystroglycanopathies, in the United States and Europe. Currently, there is no disease-modifying treatment available. Standard of care is supportive care to alleviate end organ dysfunction.

Design Criteria

The rationale for developing BBP-418 as a potential treatment for LGMD2I is based on our understanding of the disease mechanism. In healthy tissue, properly functioning Fukutin-Related Protein, or FKRP, glycosylates alpha-dystroglycan, or αDG. This glycosylation helps to stabilize muscle cells by binding extracellular ligands. In LGMD2I, mutated FKRP does not function properly and results in dysfunctional, hypo-glycosylated αDG in muscle cells, limiting αDG's ability to function as a "shock absorber" for muscle fibers and increasing cellular susceptibility to damage.

BBP-418 is designed to target the disease mechanism of LGMD2I by supplying supra-physiological levels of BBP-418 upstream to drive residual activity of the mutant FKRP enzyme and potentially increase αDG glycosylation levels.

Clinical Data

On October 14, 2022, we shared positive interim data from the ongoing Phase 2 clinical trial of BBP-418 in patients with LGMD2I at the 27th International Hybrid Annual Congress of the World Muscle Society. The open-label, dose-ascending Phase 2 trial enrolled 14 participants, including both ambulatory and non-ambulatory patients with LGMD2I, across three cohorts. As of August 16, 2022, based on the data after 12 months of treatment, we observed:

- Increased glycosylation αDG in all dose cohorts, with an average increase in αDG ratio of +0.21 at day 90.
- Greater than 75% reduction in creatine kinase, a key marker of muscle breakdown, sustained over 12 months.
- Improvements from baseline in the north star assessment for dysferlinopathy (0.95) and 10-meter walk test (10MWT) velocity (0.09 m/s) at 12 months.
- No treatment-related serious adverse events or dose limiting toxicities reported with 12 months of treatment.

Clinical Development Plan

Our Phase 2 clinical trial investigating BBP-418 in LGMD2I is ongoing. Following the release of top-line data from our Phase 2 trial, we have engaged with regulatory authorities to align on a Phase 3 trial design and intend to initiate a Phase 3 clinical trial in 2023.

Key Competitors

We believe BBP-418 is the only clinical-stage oral therapy disclosed to be in clinical development for potentially disease-modifying treatment of LGMD2I. There are no other oral therapies publicly known to be in development. There are two other identified companies developing gene therapies for the treatment of LGMD2I: Asklepios Biopharmaceutical, Inc. (LION-101) and Atamayo Therapeutics (ATA-001-FKRP/ATA-100).

BBP-631: Congenital Adrenal Hyperplasia

Summary

We are developing BBP-631, a AAV gene transfer product candidate, for the treatment of CAH, caused by 21OHD. BBP-631 was granted fast track designation from the FDA for the treatment of congenital adrenal hyperplasia 21-hydroxylase deficiency in 2021. As of February 22, 2023, four patients have been treated at the first two dose levels (1.5e13 vg/kg and 3e13 vg/kg). We plan to provide an update from patients treated at the third dose level (6e13 vg/kg) by the end of 2023.

Market Opportunity

We believe that CAH due to 21-hydroxylase, or 21OH, deficiency has one of the five largest patient populations that may be amenable to gene therapy, and is therefore a significant commercial opportunity. Over 75,000 people are estimated to be in the addressable CAH population across the US and EU; furthermore, the unmet need is significant given the side effects associated with the present standard of care treatments.

Disease Overview

CAH is a debilitating and life-threatening disease with no available cure, despite newborn screening for the disease being conducted in every U.S. state. The disease is defined by an inability to produce cortisol and aldosterone, and an excess production of testosterone. Lack of cortisol disrupts glucose metabolism and the body's normal response to stress, leading to potentially fatal adrenal crises, while lack of aldosterone disrupts sodium retention, resulting in low blood pressure, arrhythmia and dehydration. Additionally, excess testosterone causes virilization in females, often leading to ambiguous genitalia and masculinizing features at birth. Hormonal changes during puberty compound the CAH deficiencies. Females often suffer from limited fertility and require intensive treatment before, during and after pregnancy, and up to 40% of adult males will have adrenal rest tumors that can lead to gonadal dysfunction and infertility, occasionally requiring surgery.

Over 90% of CAH cases are caused by 21OHD, a genetic defect in the CYP21A2 gene coding for the enzyme 21OH. Mutations resulting in loss of enzymatic activity of 21OH prevent conversion of progesterone into 11-deoxycorticosterone and 17-hydroxyprogesterone (17OHP) into 11-deoxycortisol, which are the precursors to aldosterone and cortisol, respectively.

CAH patients with 21OHD can be divided into two categories depending on the type of genetic mutation: classic and non-classic. We are primarily focused on treating classic patients, who have the more severe phenotype and that can be categorized into simple virilizing (approximately 25% of patients) and salt-wasting (approximately 75%) by the severity of aldosterone deficiency and level of residual 21OH enzyme activity. Patients with the salt-wasting form of disease have residual enzyme activity of 0% to 1% of normal and patients with the simple virilizing phenotype have 1% to 10% enzyme activity. All patients with the classic form require treatment at birth, as cortisol deficiency can lead to adrenal crisis as early as one to four weeks of life and can quickly lead to death. The salt-wasting form has an incidence of one in 20,000 births, while the simple virilizing form has an incidence of one in 60,000 births. Together, these translate to an estimated 600 classic patients born in the United States and Europe per year. We estimate there are more than 75,000 patients in the United States and Europe in the total addressable patient population.

Current standard of care treatments do not cure patients, but replace missing glucocorticoids, such as cortisol, and mineralocorticoids, such as aldosterone, as well as reduce excessive androgen secretion. Although glucocorticoids are the mainstay of CAH therapy, individuals respond in varying ways, and chronic use of glucocorticoids in children and adults requires careful management because of the well-known side effects of these drugs, such as Cushingoid features, metabolic disease, obesity, hypertension, growth retardation, glucose intolerance, electrolyte disturbance, bone demineralization/increased risk of fracture and delayed puberty. Clinical management of classic CAH is often a very difficult balance between hyperandrogenism and hypercortisolism.

Design Criteria

BBP-631 is an intravenously administered AAV5 gene transfer product candidate designed for the treatment of CAH due to 21OHD by replacing the 21OH enzyme in the adrenal cortex. Replacement of enzyme function has the potential to normalize flux through the pathway, simultaneously addressing the lack of cortisol and aldosterone, as well as the excess of testosterone and other androgens. Genotype-phenotype correlation studies in CAH suggest that non-classic patients, who are often asymptomatic and do not require treatment, have enzyme activity that is as little as 10% to 20% of normal individuals. We believe that an AAV gene therapy may be able to restore this level of enzymatic activity in CAH patients with both simple virilizing and salt-wasting forms of disease, providing substantial clinical impact and potentially eliminating the need for treatment with exogenous steroids. BBP-631 was granted both FDA and EMA orphan drug designation in 2018 for the treatment of CAH caused by 21OHD.

Preclinical Data

Initial preclinical activity was explored in a Cyp21 knockout mouse model using AAVrh10. An intravenous, or IV, injection of vector genomes was observed to improve multiple disease-related factors over a 15-week duration window, including an increase in body weight, a decrease in urinary progesterone (the main substrate of 21OH), and an increase in renin expression (signaling an increased capacity for salt retention).

A study in non-human primates, or NHP, comparing evaluated AAV serotypes 1, 5 and 6 identified AAV5 as the optimum serotype. We observed significant transfection in the adrenals where 21OH is synthesized. Additionally, AAV5 has relatively low seroprevalence in the human population, which may limit potential immunogenicity issues.

We have completed two sets of NHP studies designed to evaluate durability of expression, dosing/transgene expression relationships and preliminary safety. In the first set of experiments, which evaluated a lower dose of $3x10^{12}$ vector genomes per kilogram, we observed sustained increases in Cyp21 mRNA levels up to six months out. We did not observe rapid decreases in vector genome counts and mRNA levels due to adrenal cell turnover between 1.5 and six months, providing preliminary support for sustained transgene expression.

In a second set of experiments, a total of 20 NHPs were treated with BBP-631 at one of three IV doses. Vector copy number and transgene mRNA expression in the adrenal glands were analyzed at four and 12 weeks post-dosing in the low- and medium-dose arms, and at 12 and 24 weeks post-dosing in the high-dose arm. No dose-related AEs were observed at any of the doses tested at any time point.

Overall, treatment with BBP-631 resulted in high vector copy number, or VCN, and mRNA expression in the adrenal gland, suggesting strong tropism and uptake of BBP-631 for the adrenal gland. In the high-dose arm, VCNs were maintained between 12 and 24 weeks. Furthermore, mRNA levels increased between 4 and 12 weeks for the medium dose arm and were consistent between 12 and 24 weeks for the high dose arm. Researchers also saw dose-dependent increases in both VCNs and mRNA levels across the three doses tested.

Key Competitors

There are two alternative therapeutic classes being investigated for treatment of CAH. The first are corticotropin-releasing factor type 1, or CRF1, receptor antagonists. CRF1 receptor antagonists regulate the release of adrenocorticotropic hormone, or ACTH, from the pituitary gland, which stimulates androgen and cortisol synthesis in the adrenal gland. In healthy individuals, endogenous cortisol provides negative feedback to the release of ACTH, which keeps androgen synthesis well-regulated. Because this negative feedback is severely impaired in CAH patients, supraphysiologic doses of exogenous steroids are required to normalize androgen synthesis in these patients. While CRF1 receptor antagonists may regulate androgen synthesis, they do not address the lack of cortisol or aldosterone production in these patients. Therefore, steroid supplementation is still required with CRF1 receptor antagonists. Two CRF receptor antagonists, Crinecerfont (under development by Neurocrine Biosciences, Inc.) and Tildacerfont (under development by Spruce Biosciences, Inc.), are currently in Phase 3 and Phase 2b clinical trials, respectively.

The second alternative therapeutic class is ACTH receptor antagonists. Inhibition of this pathway, which is downstream of the CRF1 pathway, also results in inhibition of androgen and cortisol synthesis in the adrenal gland. However, like CRF1 receptor antagonists, ACTH inhibitors do not address the lack of cortisol or aldosterone production in these patients. CRN04904, an oral ACTH antagonist, is currently in Phase 1 clinical development by Crinetics Pharmaceuticals, Inc.

While these alternative therapeutic mechanisms attempt to address meaningful aspects of the disease by potentially reducing the need for exogenous steroids, neither is able to address the disease at its source by targeting the complete set of features that define the disease. In particular, these mechanisms cannot obviate the need to administer steroids because they do not address the body's inability to synthesize cortisol and aldosterone. In contrast, we believe enzymatic replacement by gene therapy has the potential to simultaneously address all facets of the disease by restoring proper flux through the hormonal pathways, reducing androgen production by providing alternative pathways for the precursor molecules to be converted into cortisol or aldosterone.

KRAS-Driven Cancers

Our KRAS inhibitor portfolio is focused on approaches to inhibit oncogenic RAS signaling through novel selective mechanisms for the treatment of KRAS-driven cancers. It is comprised of three main efforts:

- KRAS G12C dual inhibitor
  - BBO-8520 is the first-known, investigational small molecule to directly bind and inhibit KRAS G12C in both its active (guanosine triphosphate, or GTP, bound) and inactive (guanosine diphosphate, or GDP, bound) conformations. In binding the active state, BBO-8520 is designed to disrupt effector protein binding and downstream oncogenic signaling. As of the date of this Annual Report on Form 10-K, we are not aware of a clinical-stage KRAS G12C inhibitor that directly binds the switch II pocket and inhibits the active and oncogenic GTP-bound form of the protein. In addition to its novel dual reactivity, BBO-8520 is designed to have a significantly higher potency than first-generation KRAS G12C GDP-only inhibitors. We have shown this molecule to be active in vitro against several resistant mutants that have evolved in response to GDP-inhibitor treatment. In vivo, BBO-8520 showed differentiated activity in some PDX models and led to tumor regression. We believe this could lead to differentiated activity in cancer patients with KRAS G12C driven cancer. We plan to enter the clinic with BB-8520 dual inhibitor in 2023.
- PI3K**α**:RAS breaker
  - We are also pursuing PI3Kα:RAS breakers, investigational small molecules that are designed to block RAS driven PI3Kα activation. Currently, the only approved PI3Kα inhibitor blocks both aberrant and normal kinase activity from the protein, which results in hyperglycemia and insulin-driven resistance. Through novel protein-protein interaction inhibition, breaker molecules have the potential to deliver tumor selectivity that spares normal glucose metabolism by interfering with oncogenic signaling. In addition to treating patients currently served by PI3Kα inhibitors, we expect this novel approach to potentially have broad utility for many other patients with oncogene-driven tumors (including HER2/HER3 dependency, RAS mutant tumors, PI3Kα mutant tumors, and tumors driven by RTK activation of RAS signaling) as both a monotherapy and in combination with other agents. We anticipate development candidate selection will take place in 2023 with IND filing in 2024.
- Pan-KRAS inhibitor
  - Our pan-KRAS program is designed to target multiple KRAS mutants, including KRAS G12D and KRASG12V, which are present in a large percentage of colorectal, pancreatic and non-small cell lung cancer tumors. We have achieved in vivo target engagement and have identified lead candidates with promising oral bioavailability. Development candidate selection is planned for 2023.

KRAS is a member of the RAS family of oncogenes, which also includes HRAS and NRAS, and together comprises some of the most well-known monogenic drivers of cancer. Mutations in NRAS are frequently found in leukemia and melanoma, while HRAS is frequently mutated in bladder, thyroid, and head and neck squamous cell carcinoma. KRAS mutations are a frequent driver of a number of the largest cancer indications with high unmet medical need, including 30% of non-small cell lung cancers, 98% of pancreatic adenocarcinomas and 45% of colorectal adenocarcinomas. The most common KRAS mutations involve a change from glycine at position 12 in the protein to aspartic acid (G12D, 36% of all KRAS mutations), valine (G12V, 24%), and cysteine (G12C, 15%), but also include mutations at glycine 13 and glutamine 61. In aggregate, over 500,000 patients in the United States and Europe are diagnosed with KRAS-driven cancers, annually.

BBP-398: Targeting Multiple Oncology Indications

BBP-398 is a small molecule inhibitor of SHP2 being developed as a potential treatment of cancers driven by hyperactive receptor tyrosine kinase, or RTK, or MAPK signaling. We entered into a co-development agreement with Bristol-Myers-Squibb or BMS, in July 2021 for the development of BBP-398 in combination with nivolumab, a PD-1 inhibitor, and we entered into an exclusive license agreement with BMS in May 2022 under which Navire granted BMS exclusive rights to develop and commercialize BBP-398 in all indications worldwide, except for the People's Republic of China, Macau, Hong Kong, Taiwan, Singapore and South Korea (Asia Region).

We are currently enrolling patients in three separate Phase 1 trials (NAV-1001, NAV-1003, and NAV-1004), which we are responsible for completing per the terms of the license agreement with BMS and the clinical trial collaboration and supply agreement with Amgen Inc., entered into in January 2022, regarding the conduct of combination trials with Amgen's KRAS G12C inhibitor (sotarasib).

NAV-1001 is an ongoing monotherapy dose escalation and expansion clinical trial in patients with RAS and RTK mutations.

In 2022, we initiated NAV-1003 and NAV-1004, combination trials with BBP-398 and KRAS G12C inhibitor (sotorasib; Amgen) and PD-1 (nivolumab; BMS) inhibitors, respectively.

Additionally, LianBio is now enrolling patients in a Phase 1 monotherapy dose escalation trial in the Asian Region per our Exclusive License Agreement that we entered into in August 2020. A Phase 1 clinical trial studying BBP-398 and an EGFR inhibitor (osimertinib) will be run in China by LianBio, and is expected to initiate in 2023.

BBP-671: PKAN and Organic Acidemias

BBP-671 is an oral, small molecule, allosteric activator of pantothenate kinases that we are developing for the treatment of Pantothenate Kinase Associated Neurodegeneration, or PKAN, and Organic Acidemias, or OAs. BBP-671 is currently in Phase 1 development. The healthy volunteer portion of the Phase 1 clinical trial has been completed, demonstrating initial safety and tolerability, target engagement, and suitable PK for BBP-671. The OA cohort of the Phase 1 clinical trial is now enrolling. BBP-671 has received orphan drug designation as a treatment of propionic acidemia, or PA, and as a treatment of PKAN in the United States and the European Union. BBP-671 was also designated as a drug for a rare pediatric disease for treatment of both PKAN and PA.

PKAN is a rare genetic disorder with progressive neurodegeneration. Early onset patients typically demonstrate motor deficits with possible visual problems from retinal degeneration within six years of age. Later onset disease is heterogeneous, with psychiatric symptoms and progressive parkinsonism developing in late childhood to adulthood. The prevalence of PKAN is approximately one in 1,000,000, with between 800 to 850 patients in the United States and the European Union. There are currently no approved treatments for PKAN.

OAs are caused by mutations in enzymes that disrupt amino acid metabolism leading to acute decompensations requiring hospitalization, as well as long-term complications involving multiple organ systems, such as the heart, pancreas, kidney, liver and brain. The incidence of OAs is approximately five in 100,000 births. The standard of care includes dietary restriction and supplementation, but unmet need remains high due to metabolic decompensations and long-term complications.

BBP-812: Canavan Disease

BBP-812 is an AAV gene therapy product candidate that we are developing for the treatment of Canavan Disease. BBP-812 was granted fast track designation from the FDA for the treatment of Canavan Disease in 2021 and our Phase 1/2 clinical trial of BBP-812 for the treatment of Canavan disease is ongoing. We presented preliminary biomarker data from three patients at our low dose (1.32e13 vg/kg) on October 13, 2022, and expect to dose the first patient at our high dose (3e14 vg/kg) by the end of 2023.

Canavan Disease is a fatal, progressive neurodegenerative disorder that begins in infancy. The disease is a leukodystrophy, caused by degradation of white matter in the brain. Patients typically miss developmental milestones, have a rapidly increasing head circumference, progressive lack of motor control, and often do not live past their mid-teens. The incidence of Canavan Disease is approximately one in 100,000 births worldwide. No treatments are approved for Canavan Disease; care is focused on symptom management.

Additional Program-Related Information

Manufacturing

We do not own or operate, and currently have no plans to establish, any manufacturing facilities. We currently depend on third-party contract manufacturing organizations, or CMOs, for all of our requirements of raw materials, drug substance and drug product for our preclinical research and our ongoing clinical trials of our product candidates. Aside from a manufacturing agreement that we entered into in December 2019 through one of our subsidiaries, that was terminated by mutual agreement in May 2022, we have not entered into long-term agreements with our current CMOs. We intend to continue to rely on CMOs for later-stage development and commercialization of our product candidates, including any additional product candidates that we may identify. Although we rely on CMOs, we have personnel and third-party consultants with extensive manufacturing experience to oversee the relationships with our contract manufacturers. Several of our development candidates have or are in the near term expected to have redundant and overlapping drug substance and drug product supply chains.

Sales and Marketing

We intend to build a commercial infrastructure in the United States and selected other territories to support the commercialization of our current product candidates when we believe a regulatory approval in a particular territory is likely. Because most of our target indications are rare diseases with a concentrated prescribing audience and a small number of key opinion leaders who influence the treatments prescribed for the relevant patient population, we currently believe that we can effectively address each market using our own targeted, specialty sales and marketing organization supported by internal sales personnel, an internal marketing group and distribution support. To date, we have received regulatory approval for two products that we previously developed, TRUSELTIQ (infigratinib) for the treatment of patients with previously-treated locally advanced or metastatic cholangiocarcinoma, or CCA harboring an FGFR2 fusion or rearrangement, and NULIBRY (fosdenopterin) for injection as the first therapy to reduce the risk of mortality in patients with MoCD Type A. Sentynl Therapeutics, Inc., or Sentynl, acquired global rights to NULIBRY in the first quarter of 2022 and is now responsible for the ongoing development and commercialization of NULIBRY in the United States and developing, manufacturing and commercializing fosdenopterin globally. Following FDA approval of TRUSELTIQ (infigratinib) in May 2021, we were the principal selling party of this product in the United States. Commencing in January 2022, we sold the remaining transitional supply of TRUSELTIQ to Helsinn Healthcare S.A. and Helsinn Therapeutics (U.S.), Inc., or collectively, Helsinn, and Helsinn became the principal selling party. Helsinn announced that it will stop supplying TRUSELTIQ by March 31, 2023. In December 2022, we entered into a mutual termination agreement with Helsinn concerning, among other things, steps to wind down the commercialization of infigratinib in oncology indications. (See Note 11 to our consolidated financial statements.)

We evaluate our commercialization strategy as we advance each product candidate through clinical development and to regulatory approval. In any core markets outside of the United States that we may identify, where appropriate, we may utilize strategic partners, distributors or contract sales forces to expand the commercial availability of our product candidates, if approved. We currently do not expect that we will require large pharmaceutical partners for the commercialization of any of our product candidates, if approved, although we may consider partnering in certain territories or indications or for other strategic purposes.

Programs Prioritized for Partnership

In January 2022, we committed to a restructuring initiative that included, among other components, the reprioritization of our development programs. As part of this restructuring initiative, we plan to advance several programs only through potentially new partnerships. Some of these investigational programs are identified below.

- BBP-711, an oral, small molecule inhibitor of glycolate oxidase, for treatment of primary hyperoxaluria and patients who experience recurrent kidney stones;
- BBP-589/PTR-01, an IV administered recombinant collagen type VII, or rC7, protein replacement therapy candidate, for the treatment of recessive dystrophic epidermolysis bullosa;
- BBP-681, a transdermal P13K inhibitor, for treatment of cutaneous venous and lymphatic malformations;
- BBP-561, a topical KLK5/7 inhibitor, for treatment of Netherton Syndrome;
- BBP-472, a series of small molecule P13KB inhibitors, for treatment of children with autism spectrum disorders characterized by loss of the PTEN protein; and
- BBP-818, a preclinical AAV gene therapy product candidate, for treatment of classic galactosemia.

In addition, we have a preclinical discovery program (BBP-954) for irreversible inhibitors of glutathione peroxidase 4, or GPX4, for the treatment of solid and hematological cancers. In December 2022, our co-development partner, Helsinn, terminated our partnership for this discovery program.

Intellectual Property

Overview

We strive to protect the proprietary technology that we believe is important to our business through a variety of methods, including seeking and maintaining patents and patent applications intended to cover our product candidates and compositions, their methods of use and processes for their manufacture, our platform technologies and any other aspects of inventions that are commercially important to the development of our business. We seek to obtain domestic and international patent protection and, in addition to filing and prosecuting patent applications in the United States, we may file counterpart patent applications in additional countries where we believe such foreign filing is likely to be beneficial, including Australia, Canada, Europe, China, Japan, and Mexico. We have entered into various license agreements to obtain the rights to use certain patents for the development and commercialization of our product candidates. See "Our Material Agreements." We also rely on trade secrets to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection.

Our success will depend on our ability to obtain and maintain patent and other proprietary rights protecting our commercially important technology, inventions and know-how related to our business, defend and enforce our current and future issued patents, if any, preserve the confidentiality of our trade secrets and operate without infringing the valid and enforceable patents and proprietary rights of third parties. We continually assess and refine our intellectual property strategy in order to best fortify our position, and file additional patent applications when our intellectual property strategy warrants such filings. We also rely on know-how, continuing technological innovation, and potential in-licensing opportunities to develop and maintain our intellectual property portfolio. We seek to obtain domestic and international patent protection, and endeavor to promptly file patent applications for new commercially valuable inventions.

The patent positions of biopharmaceutical companies like us are generally uncertain and involve complex legal, scientific, and factual questions. In addition, the coverage claimed in a patent application can be significantly reduced before the patent is issued, and patent scope can be reinterpreted by the courts after issuance. Moreover, many jurisdictions permit third parties to challenge issued patents in administrative proceedings, which may result in further narrowing or even cancellation of patent claims. We cannot predict whether the patent applications we are currently pursuing will issue as patents in any particular jurisdiction or whether the claims of any patents, if issued, will provide sufficient protection from competitors.

Because patent applications in the United States and certain other jurisdictions are maintained in secrecy for 18 months or potentially even longer, and since publication of discoveries in the scientific or patent literature often lags behind actual discoveries, we cannot be certain of the priority of inventions covered by pending patent applications. Moreover, we may have to participate in interference proceedings or derivation proceedings declared by the United States Patent and Trademark Office, or USPTO, to determine priority of invention.

As of February 13, 2023, our intellectual property portfolio is composed of 135 issued patents and 81 patent applications that we license from academic and research institutions and other third parties, and 33 issued patents and 374 pending patent applications that we own or co-own, including through our subsidiaries. These patents and patent applications generally provide us with the rights to develop our product candidates in the United States and worldwide. Our intellectual property portfolios for each of the programs that we consider to be our core value drivers are further described below.

For our subsidiary, QED Therapeutics, Inc., we license rights from Novartis to two issued U.S. patents, and related pending and issued foreign patents and patent applications in Australia, Canada, China, Europe, Japan and Mexico, as well as in other countries in Asia and in South America, that are directed to compositions of matter of infigratinib. The foreign patents and patent applications, if issued, are expected to expire between 2025 and 2030. The issued U.S. patents are expected to expire between 2028 and 2029, which takes into account patent term adjustments granted by the USPTO as well as a terminal disclaimer of one issued patent to another U.S. patent. Upon the initial approval of infigratinib, QED applied for 1,516 days of patent term extension, or PTE, for the U.S. patent covering the infigratinib compound; assuming grant of the PTE application, the term of this patent may be extended from August 25, 2029, to October 19, 2033.

We also license rights from Novartis to two issued U.S. patents, one pending U.S. patent application, and related pending and issued foreign patents and patent applications in Australia, Canada, China, Europe, Japan and Mexico, as well as in other countries in Asia and in South America, that are directed to pharmaceutical formulations containing infigratinib. The issued patents and patent applications, if issued, are expected to expire in 2034. In addition, we license rights from Novartis to one issued U.S. patent, one pending U.S. patent application, and related pending and issued foreign patents and patent applications in Australia, Canada, China, Europe, Japan and Mexico, as well as in other countries in Asia, that are directed to methods of treating hypophosphatemic disorders. The issued patents and patent applications, if issued, are expected to expire in 2033.

We also license rights from Inserm Transfert ESA and Assistance Publique-Hôpitaux de Paris to two issued U.S. patents and one pending U.S. patent application, and one granted patent in Europe, that are directed to methods of treating skeletal dysplasias, achondroplasia using infigratinib. The issued U.S. patents, granted patent in Europe, and the pending patent application, if issued, are expected to expire in 2032.

In addition, QED Therapeutics, Inc. owns three pending U.S. patent applications, one pending Patent Cooperation Treaty, or PCT, patent application, and related pending foreign patent applications in Australia, Canada, China, Europe, Japan and Mexico, as well as in other countries in Asia, that are directed to methods of treating various cancers or skeletal disorders using infigratinib. If any patents issue from these patent applications, such patents would be expected to expire between 2040 and 2043.

For our subsidiary Eidos Therapeutics, Inc., we license rights from the Board of Trustees of the Leland Stanford Junior University, or Stanford, to ten issued U.S. patents, two pending U.S. patent applications, one issued European patent, and one issued Japanese patent with claims directed to composition of matter and methods of use relating to acoramidis. These patents are expected to expire in 2031 or 2033.

In addition, we own four issued U.S. patents, three pending U.S. patent applications, and 51 related foreign patent applications pending in various jurisdictions, including Australia, Canada, Europe, China, Japan, and Mexico, with claims directed to salt and solid forms, methods of manufacturing, dosing methods, and formulations relating to acoramidis. The issued U.S. patents are expected to expire in 2038 or 2039. The pending U.S. and foreign patent applications, if issued, are also expected to expire in 2038 or 2039.

For our subsidiary Adrenas Therapeutics, Inc., we own one pending U.S. patent application, one pending PCT patent application, and six related foreign patent applications pending in various jurisdictions including Canada, China, Europe, Japan, and Korea with claims directed to recombinant AAV vectors relating to BBP-631 and dosing of the same. These patent applications, if issued, are expected to expire in 2039 or 2042.

Our subsidiary TheRas, Inc. co-owns with Leidos Biomedical Research, Inc., or Leidos, and Lawrence Livermore National Security, LLC, or Livermore, six pending U.S. patent applications, four pending PCT applications, and eight pending foreign applications with claims directed to modulators of K-RAS, which include claims to the modulators as composition of matter and their use in therapy, including the treatment of cancer. Any patents issuing from these applications are expected to expire between 2042 and 2044. In addition, TheRas co-owns with Leidos and Livermore one pending U.S. patent application, one pending PCT application, and two pending foreign applications with claims directed to compounds that may disrupt interactions between PI3Kα and small GTPases, which include claims to the compounds as composition of matter and their use in therapy, including the treatment of cancer. Any patents issuing from these applications are expected to expire in 2043.

Our Material Agreements

Acoramidis

License Agreement with Alexion

In September 2019, through our subsidiary Eidos Therapeutics, Inc., or Eidos, we entered into a license agreement, or the Alexion License Agreement, with Alexion Pharma International Operations Unlimited Company, a subsidiary of Alexion Pharmaceuticals, Inc., or together, Alexion, to develop and commercialize acoramidis in Japan. Additionally, in September 2019, Eidos entered into a stock purchase agreement with Alexion, pursuant to which Eidos sold to Alexion 556,173 shares of its common stock for aggregate cash proceeds of $25.0 million. Under the terms of the Alexion License Agreement, Eidos granted Alexion an exclusive license to certain of our intellectual property rights to develop, manufacture and commercialize acoramidis in Japan. In consideration for the license grant, Eidos received an upfront payment of $25.0 million, with the potential for an additional one-time payment of $30.0 million subject to the achievement of a regulatory milestone. In addition, Eidos is entitled to receive royalties in the low double-digits on net sales by Alexion of acoramidis in Japan. The royalty rate is subject to reduction if Alexion is required to obtain intellectual property rights from third parties to develop, manufacture or commercialize acoramidis in Japan, or upon the introduction of generic competition into the market.

License Agreement with the Board of Trustees of the Leland Stanford Junior University

In April 2016, through Eidos, we entered into an exclusive license agreement with Stanford for rights relating to novel transthyretin aggregation inhibitors. Under our agreement, Stanford has granted us an exclusive worldwide license to make, use and sell products that are covered by the licensed patent rights. This license grant expires when the last licensed patent expires. The patent rights exclusively licensed to us under the license are described in more detail above under the heading “Intellectual property— Eidos Therapeutics, Inc.”

Stanford retains the right, on behalf of itself and all other non-profit academic research institutions, to practice under the patent rights for any non-profit purpose, including sponsored research and collaborations. We may grant sublicenses to third parties so long as we are actively pursuing the development or commercialization of products covered by the patent rights. We may also be required to sublicense our rights under the agreement at Stanford’s request under certain conditions, including if we are unwilling or unable to serve a potential market or territory and there is a third party willing to be a sublicensee in such market or territory.

We are obligated to pay to Stanford a yearly license maintenance fee during the term of the agreement, but we may offset the maintenance fee against earned royalty payments due on net sales occurring in that year. Stanford is entitled to receive a royalty as a percentage of net sales of licensed products, in the low single digits. We have agreed to pay Stanford a percentage of non-royalty revenue we receive from our sublicensees, with the amount owed decreasing annually for three years based on when we enter into the applicable sublicense agreement. In addition, we are obligated to pay Stanford up to approximately $1.0 million upon the achievement of specific intellectual property, clinical and regulatory milestone events. In the event of a change of control transaction with respect to Eidos, we are obligated to pay Stanford a change of control fee of $250,000 in connection with the assignment of the license agreement to the acquirer of Eidos.

Under the license agreement with Stanford, we are obligated to use commercially reasonable efforts to develop, manufacture, and commercialize at least one licensed product; to develop markets for such licensed products; and to meet certain development milestones as agreed upon between us and Stanford.

Subject to the expiration of the license grant described above, the agreement does not have a specified term. We may terminate the agreement by providing prior written notice to Stanford, and Stanford has the right to terminate the agreement if we fail to achieve certain milestones or make payments under the agreement, or are not actively pursuing development of a licensed product, or if we otherwise materially breach the agreement and fail to cure such breach within a specified grace period.

Infigratinib: License Agreement with Novartis International Pharmaceutical Ltd.

In January 2018, through our subsidiary QED Therapeutics, Inc., or QED, we entered into a license agreement with Novartis International Pharmaceutical Ltd., or Novartis, for certain intellectual property rights, including patents and know-how, related to infigratinib for the treatment of patients with FGFR-driven diseases, including CCA, UC and achondroplasia. We refer to this agreement as the Novartis License.

Pursuant to the Novartis License, we obtained a license to research, develop, make, have made, use, import, offer for sale, sell, have sold and otherwise commercialize infigratinib, as well as therapeutic products incorporating infigratinib that would, but for the license grant, infringe Novartis' license patent rights, or that were developed using or that incorporate or embody Novartis' licensed know-how, in all fields of use worldwide. The license grant to us includes the right to sublicense through multiple tiers. We also have certain rights to intellectual property licensed to Novartis' affiliate under a materials transfer agreement with a third party.

The Novartis License is subject to Novartis' existing obligations to supply a third party with infigratinib to support the third party's clinical trials, and we have an ongoing obligation to inform Novartis of our or our sublicensees' intent to seek regulatory approval for and commercialize infigratinib for various indications, with potential reversionary rights to Novartis in the event of a subsequent decision not to seek regulatory approval and commercialization, or a determination by Novartis that we have failed to sufficiently pursue regulatory approval and commercialization, for Novartis to grant such third party limited rights to develop and commercialize infigratinib.

Under the terms of the Novartis License, we made a one-time payment of $15.0 million to Novartis and agreed to issue shares of Series A preferred stock of QED valued at approximately $1.7 million in the aggregate to Novartis. In addition, we are obligated to make contingent milestone payments totaling $60.0 million upon achievement of certain regulatory milestones. We are also obligated to make contingent milestone payments totaling $35.0 million upon achievement of certain sales milestones for therapeutic products incorporating infigratinib. QED also agreed to pay Novartis tiered low double-digit royalties on net sales of therapeutic products incorporating infigratinib. Following the FDA's approval of TRUSELTIQ in May 2021, we paid a one-time regulatory milestone payment to Novartis of $20.0 million.

Under the Novartis License, we are required to use commercially reasonable efforts to develop infigratinib, and to obtain regulatory approval for and commercialize infigratinib in the United States and the European Union.

We may terminate the Novartis License in its entirety or on a product-by-product or country-by-country basis at any time with 60 days' prior written notice to Novartis. Novartis may terminate if QED ceases to function as a going concern, is the subject of certain bankruptcy or similar proceedings, or otherwise winds down or discontinues its business. Either party may terminate for material breach that is not cured by the other party within a specified time period of receiving notice of such material breach. Otherwise, the Novartis License terminates on a product-by-product and country-by-country basis on the latest of the expiration of licensed patent rights, the expiration of regulatory exclusivity, or the tenth anniversary of the first commercial sale in such country.

Fosdenopterin: Asset Purchase Agreement with Alexion Pharma Holding Unlimited Company

In June 2018, through our subsidiary Origin Biosciences, Inc., we entered into an asset purchase agreement with Alexion Pharma Holding Unlimited Company, or Alexion Pharma, pursuant to which we acquired Alexion's right, title and interest in certain assets relating to fosdenopterin, including patents and other intellectual property rights.

In the event that a priority review voucher is granted to us by the FDA, we have agreed to pay Alexion Pharma a percentage in the mid-teens of any proceeds received by us from our sale of the PRV to a third party. If we do not sell the PRV to a third party within 180 days after our receipt of the PRV, we are obligated to pay Alexion Pharma $18.8 million, which amount is creditable against any amounts otherwise due to Alexion Pharma in accordance with the preceding sentence upon any future sale by us of the PRV. We are obligated to make contingent milestone payments totaling $3.0 million upon achievement of certain development milestones and $17.0 million upon achievement of certain sales milestones for products containing the fosdenopterin molecule. We also agreed to pay Alexion Pharma tiered royalties ranging from the low-to mid-teens on net sales of products containing the fosdenopterin molecule.

In 2021, we paid Alexion a $2.0 million regulatory milestone upon the FDA's approval of NULIBRY, a $1.0 million sales-based milestone payment, and $15.0 million as a result of the sale of the PRV to Eidos.

We are obligated to use commercially reasonable efforts to obtain a PRV, achieve specified milestone events and commercialize at least one product containing the fosdenopterin molecule after receipt of regulatory approval.

BBP-398: License Development and Commercialization Agreement with Bristol-Myers Squibb Company

On May 12, 2022, BridgeBio and our subsidiary, Navire Pharma, Inc., or Navire, entered into an exclusive license development and commercialization agreement with Bristol-Myers Squibb Company, or BMS, pursuant to which Navire granted BMS exclusive rights to develop and commercialize Navire's product candidate, BBP-398, in all indications worldwide, except for the People's Republic of China, Macau, Hong Kong, Taiwan, Thailand, Singapore, and South Korea, or collectively, the Asia Region. We refer to this agreement as the Navire-BMS License Agreement.

Under the terms of the Navire-BMS License Agreement, Navire was entitled to receive a non-refundable, upfront payment of $90.0 million, which Navire collected in full in June 2022. Additionally, Navire is eligible to receive additional payments totaling up to approximately $815.0 million in the aggregate, subject to the achievement of development, regulatory and commercial milestones, as well as tiered royalties in the low-to-mid teens as a percentage of adjusted net sales by BMS of the licensed products sold worldwide, outside of the Asia Region. Navire will retain the option to acquire higher royalties in the United States in connection with funding a portion of development costs upon the initiation of registrational studies. Based on the terms of the Navire-BMS License Agreement, Navire will continue to lead its ongoing Phase 1 monotherapy and combination therapy trials and BMS will lead and fund all other development and commercialization activities.

Government Regulation

Government authorities in the United States at the federal, state and local level and in other countries regulate, among other things, the research, development, manufacture, testing, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, post-approval monitoring and reporting, marketing and export and import of drug and biological products, including gene therapies, as well as diagnostics, and any future product candidates. Generally, before a new drug, biologic or diagnostic can be marketed, considerable data demonstrating its quality, safety and efficacy must be obtained, organized into a format specific for each regulatory authority, submitted for review and approved, authorized, or cleared by the applicable regulatory authority.

U.S. Government Regulation of Drug and Biological Products

In the United States, the FDA regulates drugs under the Federal Food, Drug and Cosmetic Act, or FDCA, and its implementing regulations and biologics under the FDCA and the Public Health Service Act, or PHSA, and their implementing regulations. Both drugs and biologics also are subject to other federal, state and local statutes and regulations, such as those related to competition. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, and local statutes and regulations requires the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or following approval may subject an applicant to administrative actions or judicial sanctions. These actions and sanctions could include, among other actions, the FDA's refusal to approve pending applications, withdrawal of an approval, license revocation, a clinical hold, untitled or warning letters, voluntary or mandatory product recalls or market withdrawals, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement and civil or criminal fines or penalties. Any agency or judicial enforcement action could have a material adverse effect on our business, the market acceptance of our product candidates, if approved, and our reputation.

Our product candidates must be approved by the FDA through either a New Drug Application, or NDA or a Biologics License Application, or BLA, process before they may be legally marketed in the United States. The process generally involves the following:

- completion of extensive preclinical studies in accordance with applicable regulations, including studies conducted in accordance with Good Laboratory Practices, or GLP, requirements;
- submission to the FDA of an IND, which must become effective before human clinical trials may begin;
- approval by an Institutional Review Board, or IRB, or independent ethics committee at each clinical trial site before each human trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with applicable IND regulations, Good Clinical Practices, or GCP, requirements and other clinical trial-related regulations to establish the safety and efficacy of the investigational product for each proposed indication;
- submission to the FDA of an NDA or BLA;
- a determination by the FDA within 60 days of its receipt of an NDA or BLA to accept the filing for review;
- satisfactory completion of one or more FDA pre-approval inspections of the manufacturing facility or facilities where the drug or biologic will be produced to assess compliance with Current Good Manufacturing Practices, or cGMP, requirements to assure that the facilities, methods and controls are adequate to preserve the drug or biologic's identity, strength, quality and purity;
- potential FDA audit of the clinical trial sites that generated the data in support of the NDA or BLA;
- payment of user fees for FDA review of the NDA or BLA; and
- FDA review and approval of the NDA or BLA, including consideration of the views of any FDA advisory committee, prior to any commercial marketing or sale of the drug or biologic in the United States.

The preclinical and clinical testing and approval process requires substantial time, effort and financial resources, and the regulatory scheme for drugs and biologics is evolving and subject to change at any time. We cannot be certain that any approvals for our product candidates will be granted on a timely basis, or at all.

Preclinical Studies

Before testing any drug, biological or gene therapy candidate in humans, the product candidate must undergo rigorous preclinical testing. Preclinical studies include laboratory evaluation of product chemistry and formulation, as well as *in vitro* and animal studies to assess safety and in some cases to establish a rationale for therapeutic use. The conduct of preclinical studies is subject to federal and state regulations and requirements, including GLP regulations for safety/toxicology studies.

An IND sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical trials, among other things, to the FDA as part of an IND. An IND is a request for authorization from the FDA to administer an investigational product to humans, and must become effective before human clinical trials may begin. Some long-term preclinical testing, such as animal tests of reproductive AEs and carcinogenicity, may continue after the IND is submitted. An IND automatically becomes effective 30 days after receipt by the FDA, unless before that time, the FDA raises concerns or questions related to one or more proposed clinical trials and places the trial on clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. As a result, submission of an IND may not result in the FDA allowing clinical trials to commence. Additionally, the review of information in an IND submission may prompt FDA to, among other things, scrutinize existing INDs or any marketed products and could generate requests for information or clinical holds on other product candidates or programs.

Clinical Trials

The clinical stage of development involves the administration of the investigational product to healthy volunteers or patients under the supervision of qualified investigators, generally physicians not employed by or under the trial sponsor’s control, in accordance with GCP requirements, which include the requirement that all research subjects provide their informed consent for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria and the parameters to be used to monitor subject safety and assess efficacy. Each protocol, and any subsequent amendments to the protocol, must be submitted to the FDA as part of the IND. Furthermore, each clinical trial must be reviewed and approved by an IRB for each institution at which the clinical trial will be conducted to ensure that the risks to individuals participating in the clinical trials are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the informed consent form that must be provided to each clinical trial subject or his or her legal representative, and must monitor the clinical trial until completed. There also are requirements governing the reporting of ongoing clinical trials and completed clinical trial results to public registries. Information about certain clinical trials, including clinical trial results, must be submitted within specific timeframes for publication on the www.clinicaltrials.gov website.

In addition to the submission of an IND to the FDA before initiation of a clinical trial in the United States, certain human clinical trials involving recombinant or synthetic nucleic acid molecules are subject to oversight by institutional biosafety committees, or IBC's, as set forth in the NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules, or NIH Guidelines. Under the NIH Guidelines, recombinant and synthetic nucleic acids are defined as (i) molecules that are constructed by joining nucleic acid molecules and that can replicate in a living cell (i.e., recombinant nucleic acids); (ii nucleic acid molecules that are chemically or by other means synthesized or amplified, including those that are chemically or otherwise modified but can base pair with naturally occurring nucleic acid molecules (i.e., synthetic nucleic acids); or (iii) molecules that result from the replication of those described in (i) or (ii). Specifically, under the NIH Guidelines, supervision of human gene transfer trials includes evaluation and assessment by an 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 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.

A sponsor who wishes to conduct a clinical trial outside of the United States may, but need not, obtain FDA authorization to conduct the clinical trial under an IND. If a foreign clinical trial is not conducted under an IND, the sponsor may submit data from the clinical trial to the FDA in support of an NDA or BLA. The FDA will accept a well-designed and well-conducted foreign clinical study not conducted under an IND if the study was conducted in accordance with GCP requirements, and the FDA is able to validate the data through an onsite inspection if deemed necessary.

Clinical trials generally are conducted in three sequential phases, known as Phase 1, Phase 2 and Phase 3, and may overlap.

- Phase 1 clinical trials generally involve a small number of healthy volunteers or disease-affected patients who are initially exposed to a single dose and then multiple doses of the product candidate. The primary purpose of these clinical trials is to assess the metabolism, pharmacologic action, side effect tolerability and safety of the product candidate.
- Phase 2 clinical trials involve studies in disease-affected patients to evaluate proof of concept and/or determine the dose required to produce the desired benefits. At the same time, safety and further PK and PD information is collected, possible adverse effects and safety risks are identified, and a preliminary evaluation of efficacy is conducted.
- Phase 3 clinical trials generally involve a large number of patients at multiple sites and are designed to provide the data necessary to demonstrate the effectiveness of the product for its intended use, its safety in use and to establish the overall benefit/risk relationship of the product and provide an adequate basis for product labeling.

Post-approval trials, sometimes referred to as Phase 4 clinical trials, may be conducted after initial marketing approval. These trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication and are commonly intended to generate additional safety data regarding use of the product in a clinical setting. In certain instances, the FDA may mandate the performance of Phase 4 clinical trials as a condition of approval of an NDA or BLA.

Progress reports detailing the results of the clinical trials, among other information, must be submitted at least annually to the FDA and written IND safety reports must be submitted to the FDA and the investigators 15 days after the trial sponsor determines the information qualifies for reporting for serious and unexpected suspected AEs, findings from other studies or animal or *in vitro* testing that suggest a significant risk for human subjects and any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. The sponsor must also notify the FDA of any unexpected fatal or life-threatening suspected adverse reaction as soon as possible but in no case later than seven calendar days after the sponsor's initial receipt of the information.

Phase 1, Phase 2, Phase 3 and other types of clinical trials may not be completed successfully within any specified period, if at all. The FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug or biologic has been associated with unexpected serious harm to patients. Additionally, some clinical trials are overseen by an independent group of qualified experts organized by the clinical trial sponsor, known as a data safety monitoring board or committee. This group provides authorization for whether a trial may move forward at designated check points based on access to certain data from the trial. Concurrent with clinical trials, companies usually complete additional animal studies and also must develop additional information about the chemistry and physical characteristics of the drug or biologic as well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product and, among other things, companies must develop methods for testing the identity, strength, quality and purity of the final product. Additionally, appropriate packaging must be selected and tested, and stability studies must be conducted to demonstrate that the product candidates do not undergo unacceptable deterioration over their shelf life.

FDA Review Process

Following completion of the clinical trials, data are analyzed to assess whether the investigational product is safe and effective for the proposed indicated use or uses. The results of preclinical studies and clinical trials are then submitted to the FDA as part of an NDA or BLA, along with proposed labeling, chemistry and manufacturing information to ensure product quality and other relevant data. The NDA or BLA is a request for approval to market the drug or biologic for one or more specified indications and must contain proof of safety and efficacy for a drug or safety, purity and potency for a biologic. The application may include both negative and ambiguous results of preclinical studies and clinical trials, as well as positive findings. Data may come from company-sponsored clinical trials intended to test the safety and efficacy of a product's use or from a number of alternative sources, including studies initiated by investigators. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety and efficacy of the investigational product to the satisfaction of FDA. FDA approval of an NDA or BLA must be obtained before a drug or biologic may be marketed in the United States.

Under the Prescription Drug User Fee Act, or PDUFA, as amended, each NDA or BLA must be accompanied by a user fee. FDA adjusts the PDUFA user fees on an annual basis. Fee waivers or reductions are available in certain circumstances, including a waiver of the application fee for the first application filed by a small business. Additionally, no user fees are assessed on NDAs or BLAs for products designated as orphan drugs, unless the product also includes a non-orphan indication.

The FDA reviews all submitted NDAs and BLAs before it accepts them for filing, and may request additional information rather than accepting the NDA or BLA for filing. The FDA must make a decision on accepting an NDA or BLA for filing within 60 days of receipt, and such decision could include a refusal to file by the FDA. Once the submission is accepted for filing, the FDA begins an in-depth review of the NDA or BLA. Under the goals and policies agreed to by the FDA under PDUFA, the FDA targets ten months, from the filing date, in which to complete its initial review of a new molecular entity NDA or original BLA and respond to the applicant, and six months from the filing date of a new molecular entity NDA or original BLA designated for priority review. The FDA does not always meet its PDUFA goal dates for standard and priority NDAs or BLAs, and the review process is often extended by FDA requests for additional information or clarification.

The FDA has developed the Oncology Center of Excellence Real-Time Oncology Review, or RTOR, pilot program to facilitate a more efficient review process for certain oncology product candidates. Although this program allows FDA to begin reviewing clinical data prior to submission of a complete NDA or BLA, the program is not intended to change the PDUFA review timelines.

Before approving an NDA or BLA, the FDA will conduct a pre-approval inspection of the manufacturing facilities for the new product to determine whether they comply with cGMP requirements. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. The FDA also may audit data from clinical trials to ensure compliance with GCP requirements. Additionally, the FDA may refer applications for novel products or products which present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved and under what conditions, if any. The FDA is not bound by recommendations of an advisory committee, but it considers such recommendations when making decisions on approval. The FDA likely will reanalyze the clinical trial data, which could result in extensive discussions between the FDA and the applicant during the review process. After the FDA evaluates an NDA or BLA, it will issue an approval letter or a Complete Response Letter. An approval letter authorizes commercial marketing of the drug or biologic with specific prescribing information for specific indications. A Complete Response Letter indicates that the review cycle of the application is complete, and the application will not be approved in its present form. A Complete Response Letter usually describes all of the specific deficiencies in the NDA or BLA identified by the FDA. The Complete Response Letter may require the applicant to obtain additional clinical data, including the potential requirement to conduct additional pivotal Phase 3 clinical trial(s) and/or to complete other significant and time-consuming requirements related to clinical trials, or to conduct additional preclinical studies or manufacturing activities. If a Complete Response Letter is issued, the applicant may either resubmit the NDA or BLA, addressing all of the deficiencies identified in the letter, or withdraw the application or request an opportunity for a hearing. Even if such data and information are submitted, the FDA may decide that the NDA or BLA does not satisfy the criteria for approval. Data obtained from clinical trials are not always conclusive and the FDA may interpret data differently than we interpret the same data.

Orphan Drug Designation and Exclusivity

Under the Orphan Drug Act, the FDA may grant orphan drug designation to a drug or biological product intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000 individuals in the United States, or 200,000 or more individuals in the United States and for which there is no reasonable expectation that the cost of developing and making the product available in the United States for this type of disease or condition will be recovered from sales of the product.

Orphan drug designation must be requested before submitting an NDA or BLA. After the FDA grants orphan drug designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If a product that has orphan drug 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 indication for seven years from the date of such approval, except in limited circumstances, such as a showing of clinical superiority to the product with orphan exclusivity by means of greater effectiveness, greater safety or providing a major contribution to patient care or in instances of drug supply issues. Competitors, however, may receive approval of either a different product for the same indication or the same product for a different indication but that could be used off-label in the orphan indication. Orphan drug exclusivity also could block the approval of our products for seven years if a competitor obtains approval before we do for the same product, as defined by the FDA, for the same indication we are seeking approval, or if our product is determined to be contained within the scope of the competitor's product for the same indication or disease. If we pursue marketing approval for an indication broader than the orphan drug designation we have received, we may not be entitled to orphan drug exclusivity. Orphan drug status in the European Union has similar, but not identical, requirements and benefits.

Rare Pediatric Disease Designation and Priority Review Vouchers

Under the FDCA, as amended, the FDA incentivizes the development of drugs and biologics that meet the definition of a "rare pediatric disease," defined to mean a serious or life-threatening disease in which the serious of life-threatening manifestations primarily affect individuals aged from birth to 18 years and the disease affects fewer than 200,000 individuals in the United States or affects more than 200,000 in the United States and for which there is no reasonable expectation that the cost of developing and making in the United States a drug for such disease or condition will be received from sales in the United States of such drug. The sponsor of a product candidate for a rare pediatric disease may be eligible for a voucher that can be used to obtain a priority review for a subsequent human drug or biologic application after the date of approval of the rare pediatric disease drug product, referred to as a priority review voucher, or PRV. A sponsor may request rare pediatric disease designation from the FDA prior to the submission of its NDA or BLA. A rare pediatric disease designation does not guarantee that a sponsor will receive a PRV upon approval of its NDA or BLA. Moreover, a sponsor who chooses not to submit a rare pediatric disease designation request may nonetheless receive a PRV upon approval of their marketing application if they request such a voucher in their original marketing application and meet all of the eligibility criteria. If a PRV is received, it may be sold or transferred an unlimited number of times. Congress has extended the PRV program through September 30, 2024, with the potential for PRVs to be granted through September 30, 2026.

Expedited Development and Review Programs

A sponsor may seek to develop and obtain approval of its product candidates under programs designed to accelerate the development, FDA review and approval of new drugs and biologics that meet certain criteria. For example, the FDA has a fast track program that is intended to expedite or facilitate the process for reviewing new drugs and biologics that are intended to treat a serious or life threatening disease or condition and demonstrate the potential to address unmet medical needs for the condition. Fast track designation applies to both the product and the specific indication for which it is being studied. For a fast track-designated product, the FDA may consider sections of the NDA or BLA for review on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the application, the FDA agrees to accept sections of the application and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the application. The sponsor can request the FDA to designate the product for fast track status any time before receiving NDA or BLA approval, but ideally no later than the pre-NDA or pre-BLA meeting.

A product submitted to the FDA for marketing, including under a fast track program, may be eligible for other types of FDA programs intended to expedite development or review, such as priority review and accelerated approval. Priority review means that, for a new molecular entity or original BLA, the FDA sets a target date for FDA action on the marketing application at six months after accepting the application for filing as opposed to ten months. A product is eligible for priority review if it is designed to treat a serious or life-threatening disease condition and, if approved, would provide a significant improvement in safety and effectiveness compared to available therapies. The FDA will attempt to direct additional resources to the evaluation of an application for a new drug or biologic designated for priority review in an effort to facilitate the review. If criteria are not met for priority review, the application for a new molecular entity or original BLA is subject to the standard FDA review period of ten months after FDA accepts the application for filing. Priority review designation does not change the scientific/medical standard for approval or the quality of evidence necessary to support approval.

Under the Food and Drug Omnibus Reform Act of 2022, or FDORA, a platform technology incorporated within or utilized by a drug or biologic is eligible for designation as a designated platform technology if (1) the platform technology is incorporated in, or utilized by, a drug approved under an NDA or BLA; (2) preliminary evidence submitted by the sponsor of the approved or licensed drug, or a sponsor that has been granted a right of reference to data submitted in the application for such drug, demonstrates that the platform technology has the potential to be incorporated in, or utilized by, more than one drug without an adverse effect on quality, manufacturing, or safety; and (3) data or information submitted by the applicable person indicates that incorporation or utilization of the platform technology has a reasonable likelihood to bring significant efficiencies to the drug development or manufacturing process and to the review process. A sponsor may request the FDA to designate a platform technology as a designated platform technology concurrently with, or at any time after, submission of an IND application for a drug that incorporates or utilizes the platform technology that is the subject of the request. If so designated, the FDA may expedite the development and review of any subsequent original NDA or BLA for a drug that uses or incorporates the platform technology. Designated platform technology status does not ensure that a drug will be developed more quickly or receive a faster FDA review process or ultimate FDA approval. In addition, the FDA may revoke a designation if the FDA determines that a designated platform technology no longer meets the criteria for such designation.

A product may also be eligible for accelerated approval if it is designed to treat a serious or life-threatening disease or condition and generally provides a meaningful advantage over available therapies upon a determination that the product has an effect on either a surrogate or intermediate clinical endpoint that is reasonably likely to predict clinical benefit or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, or IMM, that is reasonably likely to predict an effect on IMM or other clinical benefit, taking into account the severity, rarity, or prevalence of the disease or condition and the availability or lack of alternative treatments. As a condition of approval, the FDA may require that a sponsor of a drug or biologic receiving accelerated approval perform adequate and well-controlled post-marketing confirmatory clinical trials with due diligence and, under FDORA, the FDA is permitted to require, as appropriate, that such confirmatory studies be underway prior to approval or within a specified time period after accelerated approval is granted. In addition, the FDA currently requires, unless otherwise informed by the agency, pre-approval of promotional materials, which could adversely impact the timing of the commercial launch of the product. Under FDORA, the FDA has increased authority for expedited procedures to withdraw approval of a drug or indication approved under accelerated approval if, for example, the confirmatory trial fails to verify the predicted clinical benefit of the product.

Additionally, a drug or biologic may be eligible for designation as a breakthrough therapy if the product is intended, alone or in combination with one or more other drugs or biologics, to treat a serious or life-threatening condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over currently approved therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. If the FDA designates a breakthrough therapy, it may take actions appropriate to expedite the development and review of the application, which may include holding meetings with the sponsor and the review team throughout the development of the therapy; providing timely advice to, and interactive communication with, the sponsor regarding the development of the drug to ensure that the development program to gather the nonclinical and clinical data necessary for approval is as efficient as practicable; involving senior managers and experienced review staff, as appropriate, in a collaborative, cross-disciplinary review; assigning a cross-disciplinary project lead for the FDA review team to facilitate an efficient review of the development program and to serve as a scientific liaison between the review team and the sponsor; and considering alternative clinical trial designs when scientifically appropriate, which may result in smaller trials or more efficient trials that require less time to complete and may minimize the number of patients exposed to a potentially less efficacious treatment. Breakthrough therapy designation comes with all of the benefits of fast track designation, which means that the sponsor may file sections of the BLA for review on a rolling basis if certain conditions are satisfied, including an agreement with the FDA on the proposed schedule for submission of portions of the application and the payment of applicable user fees before the FDA may initiate a review.

As part of the 21st Century Cures Act, Congress amended the FDCA to facilitate an efficient development program for, and expedite review of regenerative medicine advanced therapies, or RMATs, which include cell and gene therapies, therapeutic tissue engineering products, human cell and tissue products, and combination products using any such therapies or products. RMATs do not include those human cells, tissues, and cellular and tissue based products regulated solely under section 361 of the PHSA and 21 CFR Part 1271. This program is intended to facilitate efficient development and expedite review of regenerative medicine therapies, which are intended to treat, modify, reverse, or cure a serious or life-threatening disease or condition and qualify for RMAT designation. A sponsor may request that the FDA designate a product candidate as a RMAT concurrently with or at any time after submission of an IND. The FDA has 60 calendar days to determine whether the product candidate meets the criteria, including whether there is preliminary clinical evidence indicating that the product candidate has the potential to address unmet medical needs for a serious or life-threatening disease or condition. A BLA for a product candidate that has received RMAT designation may be eligible for priority review or accelerated approval through use of surrogate or intermediate endpoints reasonably likely to predict long-term clinical benefit, or reliance upon data obtained from a meaningful number of sites. Benefits of RMAT designation also include early interactions with FDA to discuss any potential surrogate or intermediate endpoint to be used to support accelerated approval. A product candidate with RMAT designation that is granted accelerated approval and is subject to post-approval requirements may fulfill such requirements through the submission of clinical evidence from clinical studies, patient registries, or other sources of real world evidence, such as electronic health records; the collection of larger confirmatory data sets; or post-approval monitoring of all patients treated with such therapy prior to its approval.

The FDA has also announced the availability of the RTOR pilot program for oncology product candidates that are likely to demonstrate substantial improvements over available therapy, which may include drugs previously granted breakthrough therapy designation for the same or other indications and candidates meeting other criteria for other expedited programs, such as fast track and priority review. Submissions for RTOR consideration should also have straightforward study designs and endpoints that can be easily interpreted (such as overall survival or progression free survival). Acceptance into the RTOR program does not guarantee or influence approvability of the application, which is subject to the usual benefit-risk evaluation by FDA reviewers, but the program allows FDA to review data earlier, before an applicant formally submits a complete application. The RTOR program does not affect FDA's PDUFA timelines.

Even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or the time period for FDA review or approval may not be shortened. Furthermore, fast track designation, priority review, accelerated approval, breakthrough therapy and RMAT designation do not change the standards for approval.

Pediatric Information and Pediatric Exclusivity

Under the Pediatric Research Equity Act, or PREA, certain NDAs and BLAs and certain supplements to an NDA or BLA must contain data to assess the safety and efficacy of the drug for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may grant deferrals for submission of pediatric data or full or partial waivers. The Food and Drug Administration Safety and Innovation Act, or FDASIA, amended the FDCA to require that a sponsor who is planning to submit a marketing application for a drug that includes a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration submit an initial Pediatric Study Plan, or PSP, within 60 days of an end-of-Phase 2 meeting or, if there is no such meeting, as early as practicable before the initiation of the Phase 3 or Phase 2/3 study. The initial PSP must include an outline of the pediatric study or studies that the sponsor plans to conduct, including study objectives and design, age groups, relevant endpoints and statistical approach, or a justification for not including such detailed information, and any request for a deferral of pediatric assessments or a full or partial waiver of the requirement to provide data from pediatric studies along with supporting information. The FDA and the sponsor must reach an agreement on the PSP. A sponsor can submit amendments to an agreed-upon initial PSP at any time if changes to the pediatric plan need to be considered based on data collected from preclinical studies, early phase clinical trials and/or other clinical development programs.

A drug or biologic product can also obtain pediatric market exclusivity in the United States. Pediatric exclusivity, if granted, adds six months to existing exclusivity periods and patent terms. This six-month exclusivity, which runs from the end of other exclusivity protection or patent term, may be granted based on the voluntary completion of a pediatric study in accordance with an FDA-issued "Written Request" for such a study.

Post-Marketing Requirements

Following approval of a new product, the manufacturer and the approved product are subject to continuing regulation by the FDA, including, among other things, monitoring and record-keeping activities, reporting of adverse experiences to applicable regulatory authorities, complying with promotion and advertising requirements, which include, among other things, standards for direct-to-consumer advertising, requirements for promotional activities on the internet, restrictions on promoting products for unapproved uses or in patient populations that are not described in the product's approved label (known as "off-label use") and limitations on industry-sponsored scientific and educational activities. Although physicians may prescribe legally available products for off-label uses, manufacturers may not market or promote such off-label uses. The FDA does not regulate the behavior of physicians in their choice of treatment, but the FDA regulations do impose stringent restrictions on manufacturers' communications regarding off-label uses. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability, including investigation by federal and state authorities. Prescription drug promotional materials must be submitted to the FDA in conjunction with their first use or first publication, and may be required to be reviewed in advance in certain circumstances such as for products that receive accelerated approval.

Further, if there are any modifications to the drug or biologic, including changes in indications, labeling or manufacturing processes or facilities, the applicant may be required to submit and obtain FDA approval of a new NDA/BLA or NDA/BLA supplement, which may require the development of additional data or preclinical studies and clinical trials. Such regulatory reviews can result in denial or modification of the planned changes, or requirements to conduct additional tests or evaluations that can substantially delay or increase the cost of the planned changes.

The FDA may also place other conditions on approvals including the requirement for a REMS, to assure the safe use of the product. If the FDA concludes a REMS is needed, the sponsor of the NDA or BLA must submit a proposed REMS. The FDA will not approve the NDA or BLA without an approved REMS, if required. A REMS could include medication guides, physician communication plans or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. Any of these limitations on approval or marketing could restrict the commercial promotion, distribution, prescription or dispensing of products. Product approvals may be withdrawn for non-compliance with regulatory requirements, if problems occur following initial marketing or if the FDA determines that the product is no longer safe or effective.

FDA regulations require that products be manufactured in specific approved facilities and in accordance with cGMP regulations. We rely, and expect to continue to rely, on third parties for the production of clinical and commercial quantities of any approved products in accordance with cGMP regulations. NDA and BLA holders using contract manufacturers, laboratories or packagers are responsible for the selection and monitoring of qualified firms, and, in certain circumstances, qualified suppliers to these firms. These manufacturers must comply with cGMP regulations that require, among other things, quality control and quality assurance, the maintenance of records and documentation and the obligation to investigate and correct any deviations from cGMP. Manufacturers and other entities involved in the manufacture and distribution of approved drugs or biologics are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP requirements and other laws. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain cGMP compliance. The discovery of violative conditions, including failure to conform to cGMP regulations, could result in enforcement actions, and the discovery of problems with a product after approval may result in restrictions on a product, manufacturer or holder of an approved NDA or BLA, including recall or withdrawal of the product from the market.

Any distribution of prescription drugs and biologics and pharmaceutical samples must comply with the U.S. Prescription Drug Marketing Act, or PDMA, and the PHSA. In addition, the Drug Supply Chain Security Act, or DSCSA, was enacted in 2013 with the aim of building an electronic system to identify and trace certain prescription drugs and biologics distributed in the United States. The DSCSA mandates phased-in and resource-intensive obligations for pharmaceutical manufacturers, wholesale distributors, and dispensers over a 10-year period that is expected to culminate in November 2023. The law's requirements include the quarantine and prompt investigation of a suspect product, to determine if it is illegitimate, notifying trading partners and the FDA of any illegitimate product, and compliance with product tracking and tracing requirements.

Once an approval is granted, the FDA may issue enforcement letters or withdraw the approval of the product if compliance with regulatory requirements and standards is not maintained or if problems occur after the drug or biologic reaches the market. Corrective action could delay drug or biologic distribution and require significant time and financial expenditures. Later discovery of previously unknown problems with a drug or biologic, including AEs of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may require revisions to the approved labeling to add new safety information, including the addition of new warning and contraindications; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

- mandated corrective advertising or communications with doctors;
- restrictions on the marketing or manufacturing of the drug or biologic, suspension of the approval, complete withdrawal of the drug from the market or product recalls;
- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve applications or supplements to approved applications, or suspension or revocation of drug or biologic approvals;
- drug or biologic seizure or detention, or refusal to permit the import or export of drugs; or
- injunctions or the imposition of civil or criminal penalties.

Regulation of Companion Diagnostics

We believe that the success of certain of our product candidates may depend, in part, on the development and commercialization of a companion diagnostic. Companion diagnostics identify patients who are most likely to benefit from a particular therapeutic product; identify patients likely to be at increased risk for serious side effects as a result of treatment with a particular therapeutic product; or monitor response to treatment with a particular therapeutic product for the purpose of adjusting treatment to achieve improved safety or effectiveness. Companion diagnostics are regulated as medical devices by the FDA. In the United States, the FDCA and its implementing regulations, and other federal and state statutes and regulations govern, among other things, medical device design and development, preclinical and clinical testing, premarket clearance or approval, registration and listing, manufacturing, labeling, storage, advertising and promotion, sales and distribution, export and import, and post-market surveillance. Unless an exemption or FDA exercise of enforcement discretion applies, diagnostic tests generally require marketing clearance or approval from the FDA prior to commercialization. The two primary types of FDA marketing authorization applicable to a medical device are premarket notification, also called 510(k) clearance, and approval of a premarket, or PMA approval.

To obtain 510(k) clearance for a medical device, or for certain modifications to devices that have received 510(k) clearance, a manufacturer must submit a premarket notification demonstrating that the proposed device is substantially equivalent to a previously cleared 510(k) device or to a preamendment device that was in commercial distribution before May 28, 1976, or a predicate device, for which the FDA has not yet called for the submission of a PMA. In making a determination that the device is substantially equivalent to a predicate device, the FDA compares the proposed device to the predicate device or predicate devices and assesses whether the subject device is comparable to the predicate device or predicate devices with respect to intended use, technology, design and other features which could affect safety and effectiveness. If the FDA determines that the subject device is substantially equivalent to the predicate device or predicate devices, the subject device may be cleared for marketing. The 510(k) premarket notification pathway generally takes from three to twelve months from the date the application is completed, but can take significantly longer.

PMA applications must be supported by valid scientific evidence, which typically requires extensive data, including technical, preclinical, clinical and manufacturing data, to demonstrate to the FDA's satisfaction the safety and effectiveness of the device. For diagnostic tests, a PMA application typically includes data regarding analytical and clinical validation studies. As part of its review of the PMA, the FDA will conduct a pre-approval inspection of the manufacturing facility or facilities to ensure compliance with the Quality System Regulation, or QSR, which requires manufacturers to follow design, testing, control, documentation and other quality assurance procedures. The FDA's review of an initial PMA application is required by statute to take between six to ten months, although the process typically takes longer, and may require several years to complete. If the FDA evaluations of both the PMA application and the manufacturing facilities are favorable, the FDA will either issue an approval letter or an approvable letter, which usually contains a number of conditions that must be met in order to secure the final approval of the PMA. If the FDA's evaluation of the PMA or manufacturing facilities is not favorable, the FDA will deny the approval of the PMA or issue a not approvable letter. A not approvable letter will outline the deficiencies in the application and, where practical, will identify what is necessary to make the PMA approvable. Once granted, PMA approval may be withdrawn by the FDA if compliance with post-approval requirements, conditions of approval or other regulatory standards is not maintained or problems are identified following initial marketing.

On July 31, 2014, the FDA issued a final guidance document addressing the development and approval process for "In Vitro Companion Diagnostic Devices." According to the guidance document, for novel therapeutic products that depend on the use of a diagnostic test and where the diagnostic device could be essential for the safe and effective use of the corresponding therapeutic product, the premarket application for the companion diagnostic device should be developed and approved or cleared contemporaneously with the therapeutic, although the FDA recognizes that there may be cases when contemporaneous development may not be possible. However, in cases where a drug cannot be used safely or effectively without the companion diagnostic, the FDA's guidance indicates it will generally not approve the drug without the approval or clearance of the diagnostic device. The FDA also issued a draft guidance in July 2016 setting forth the principles for co-development of an in vitro companion diagnostic device with a therapeutic product. The draft guidance describes principles to guide the development and contemporaneous marketing authorization for the therapeutic product and its corresponding in vitro companion diagnostic.

Once cleared or approved, the companion diagnostic device must adhere to post-marketing requirements including the requirements of FDA's quality system regulation, adverse event reporting, recalls and corrections along with product marketing requirements and limitations. Like drug and biologic makers, companion diagnostic makers are subject to unannounced FDA inspections at any time during which the FDA will conduct an audit of the product(s) and the Company's facilities for compliance with its authorities.

Biosimilars and Exclusivity

Certain of our product candidates are regulated as biologics. An abbreviated approval pathway for biological products shown to be similar to, or interchangeable with, an FDA-licensed reference biological product was created by the Biologics Price Competition and Innovation Act of 2009, or BPCI Act, as part of the ACA. This amendment to the PHSA, in part, attempts to minimize duplicative testing. Biosimilarity, which requires that the biological product be highly similar to the reference product notwithstanding minor differences in clinically inactive components and that there be no clinically meaningful differences between the product and the reference product in terms of safety, purity and potency, can be shown through analytical studies, animal studies and a clinical trial or trials. Interchangeability requires that a biological product be biosimilar to the reference product and that the product can be expected to produce the same clinical results as the reference product in any given patient and, for products administered multiple times to an individual, that the product and the reference product may be alternated or switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biological product without such alternation or switch. Complexities associated with the larger, and often more complex, structure of biological products as compared to small molecule drugs, as well as the processes by which such products are manufactured, pose significant hurdles to implementation that are still being worked out by the FDA.

A reference biological product is granted four and twelve year exclusivity periods from the time of first licensure of the product. The FDA will not accept an application for a biosimilar or interchangeable product based on the reference biological product until four years after the date of first licensure of the reference product, and the FDA will not approve an application for a biosimilar or interchangeable product based on the reference biological product until twelve years after the date of first licensure of the reference product. “First licensure” typically means the initial date the particular product at issue was licensed in the United States. Date of first licensure does not include the date of licensure of (and a new period of exclusivity is not available for) a biological product if the licensure is for a supplement for the biological product or for a subsequent application by the same sponsor or manufacturer of the biological product (or licensor, predecessor in interest, or other related entity) for a change (not including a modification to the structure of the biological product) that results in a new indication, route of administration, dosing schedule, dosage form, delivery system, delivery device or strength, or for a modification to the structure of the biological product that does not result in a change in safety, purity, or potency. Therefore, one must determine whether a new product includes a modification to the structure of a previously licensed product that results in a change in safety, purity, or potency to assess whether the licensure of the new product is a first licensure that triggers its own period of exclusivity. Whether a subsequent application, if approved, warrants exclusivity as the “first licensure” of a biological product is determined on a case-by-case basis with data submitted by the sponsor.

Other Regulatory Matters

Manufacturing, sales, promotion and other activities following product approval are also subject to regulation by numerous regulatory authorities in the United States in addition to the FDA, including the Centers for Medicare and Medicaid Services, or CMS, including the Office of Inspector General and Office for Civil Rights, other divisions of the Department of HHS, the Department of Justice, the Drug Enforcement Administration, the Consumer Product Safety Commission, the Federal Trade Commission, the Occupational Safety & Health Administration, the Environmental Protection Agency and state and local governments.

Healthcare providers, physicians, and third party payors will play a primary role in the recommendation and prescription of any products for which we obtain marketing approval. Our current and future arrangements with healthcare providers and physicians and any future arrangements with third party payers, may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute any drugs for which we obtain marketing approval. In the United States, these laws include: the federal Anti-Kickback Statute, the False Claims Act, and the federal Health Insurance Portability and Accountability Act of 1996 (HIPAA).

The Anti-Kickback Statute makes it illegal for any person, including a prescription drug manufacturer (or a party acting on its behalf), to knowingly and willfully solicit, receive, offer or pay any remuneration, directly or indirectly, in cash or in kind, that is intended to induce or reward referrals, including the purchase, recommendation, order or prescription of a particular drug, for which payment may be made under a federal healthcare program, such as Medicare or Medicaid. Violations of this law are punishable by imprisonment, criminal fines, administrative civil money penalties and exclusion from participation in federal healthcare programs. In addition, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it. Moreover, the ACA provides that 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 federal civil False Claims Act or federal civil money penalties.

Although we would not submit claims directly to payors, drug manufacturers can be held liable under federal civil and criminal false claims laws and civil monetary penalty laws, such as the federal civil False Claims Act, which imposes criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities (including manufacturers) for, among other things, knowingly presenting, or causing to be presented to federal programs (including Medicare and Medicaid) claims for items or services, including drugs, that are false or fraudulent, claims for items or services not provided as claimed, or claims for medically unnecessary items or services. Penalties for a False Claims Act violation include three times the actual damages sustained by the government, plus mandatory civil penalties for each separate false claim, the potential for exclusion from participation in federal healthcare programs and, although the federal False Claims Act is a civil statute, conduct that results in a False Claims Act violation may also implicate various federal criminal statutes. The government may deem manufacturers to have “caused” the submission of false or fraudulent claims by, for example, providing inaccurate billing or coding information to customers or promoting a product off-label. Claims which include items or services resulting from a violation of the federal Anti-Kickback Statute are false or fraudulent claims for purposes of the False Claims Act. Our future marketing and activities relating to the reporting of wholesaler or estimated retail prices for our products, if approved, the reporting of prices used to calculate Medicaid rebate information and other information affecting federal, state and third-party reimbursement for our products, if approved, and the sale and marketing of our product candidates, are subject to scrutiny under this law.

HIPAA created federal criminal statutes that prohibit among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud or to obtain, by means of false or fraudulent pretenses, representations or promises, any money or property owned by, or under the control or custody of, any healthcare benefit program, including private third party payors, knowingly and willfully embezzling or stealing from a healthcare benefit program, willfully obstructing a criminal investigation of a healthcare offense, and knowingly and willfully falsifying, concealing or covering up by trick, scheme or device, a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. Like the federal Anti-Kickback Statute 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.

The civil monetary penalties statute imposes penalties against any person or entity that, among other things, is determined to have presented or caused to be presented a claim to a federal health program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent.

We may be subject to data privacy and security regulations by both the federal government and the states in which we conduct our business. HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 (HITECH), and their implementing regulations, including the Final Omnibus Rule published in January 2013, which imposes requirements on certain covered healthcare providers, health plans, and healthcare clearinghouses, as well as their respective business associates, independent contractors, or agents of health covered entities, that perform services for them that involve the creation, maintenance, receipt, use, or disclosure of, individually identifiable health information relating to the privacy, security, and transmission of individual identifiable health information. Among other things, HITECH makes HIPAA's security standards directly applicable to business associates, defined as independent contractors or agents of covered entities, which include certain health care providers, health plans, and healthcare clearinghouses, that create, receive or obtain protected health information in connection with providing a service for or on behalf of a covered entity. 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. In addition, there may be additional federal, state, and non-U.S. laws which govern the privacy and security of health and other personal information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts. Failure to comply with these laws, where applicable, can result in the imposition of significant civil and criminal penalties.

In addition, many states in which we operate have laws that protect the privacy and security of sensitive and personal information. Certain state laws may be more stringent or broader in scope, or offer greater individual rights, with respect to sensitive and personal information than federal, international, or other state laws, and such laws may differ from each other, which may complicate compliance efforts. Where state laws are more protective than HIPAA, we must comply with the state laws we are subject to, in addition to HIPAA. In certain cases, it may be necessary to modify our planned operations and procedures to comply with these more stringent state laws. Further, in some cases where we process sensitive and personal information of individuals from numerous states, we may find it necessary to comply with the most stringent state laws applicable to any of the information. California recently enacted the California Consumer Privacy Act, or CCPA, which creates new individual privacy rights for California consumers (as defined in the law) and places increased privacy and security obligations on entities handling personal data of consumers or households. The CCPA will require covered companies to provide certain disclosures to consumers about its data collection, use and sharing practices, and to provide affected California residents with ways to opt-out of certain sales or transfers of personal information. The CCPA went into effect on January 1, 2020, and the California State Attorney General submitted final regulations for review on June 2, 2020, which were finalized and are now effective. The California State Attorney General has commenced enforcement actions against violators as of July 1, 2020. Further, a new California privacy law, the California Privacy Rights Act, or CPRA, was passed by California voters on November 3, 2020. The CPRA will create additional obligations with respect to processing and storing personal information effective January 1, 2023 (with certain provisions having retroactive effect to January 1, 2022). We will continue to monitor developments related to the CPRA and anticipate additional costs and expenses associated with CPRA compliance. Other U.S. states also are considering omnibus privacy legislation and industry organizations regularly adopt and advocate for new standards in these areas. While the CCPA and CPRA contain an exception for certain activities involving PHI under HIPAA, we cannot yet determine the impact the CCPA, CPRA or other such future laws, regulations and standards may have on our business.

Additionally, some observers have noted that the CCPA and CPRA could mark the beginning of a trend toward more stringent privacy legislation in the U.S., which could increase our potential liability and adversely affect our business. Already, in the United States, we have witnessed significant developments at the state level. For example, on March 2, 2021, Virginia enacted the Consumer Data Protection Act, or the CDPA and, on July 8, 2021, Colorado's governor signed the Colorado Privacy Act, or CPA, into law. The CDPA and the CPA both became effective January 1, 2023. While the CDPA and CPA incorporate many similar concepts of the CCPA and CPRA, there are also several key differences in the scope, application, and enforcement of the law that will change the operational practices of regulated businesses. Moreover, on March 24, 2022, Utah's governor signed the Utah Consumer Privacy Act, or UCPA, into law. The UCPA will take effect on December 31, 2023. Also, in May 2022, Connecticut Governor Ned Lamont signed the Connecticut Data Privacy Act, or CTDPA, into law. The UCPA and CTDPA draw heavily upon their predecessors in Virginia and Colorado. With the CTDPA, Connecticut became the fifth state to enact a comprehensive privacy law.

A number of other states have proposed new privacy laws, some of which are similar to the above discussed recently passed laws. Such proposed legislation, if enacted, may add additional complexity, variation in requirements, restrictions and potential legal risk, require additional investment of resources in compliance programs, impact strategies and the availability of previously useful data and could result in increased compliance costs and/or changes in business practices and policies. The existence of comprehensive privacy laws in different states in the country would make our compliance obligations more complex and costly and may increase the likelihood that we may be subject to enforcement actions or otherwise incur liability for noncompliance.

Additionally, the federal Physician Payments Sunshine Act, or the Sunshine Act, within the ACA, and its implementing regulations, require that certain manufacturers of drugs, devices, biological and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) report annually to CMS information related to certain payments or other transfers of value made or distributed to physicians and teaching hospitals, or to entities or individuals at the request of, or designated on behalf of, physicians, certain other healthcare professionals, and teaching hospitals and to report annually certain ownership and investment interests held by physicians, certain other healthcare professionals, and their immediate family members. Effective January 1, 2022, these reporting obligations extend to include transfers of value made to certain non-physician providers such as physician assistants and nurse practitioners. In addition, many states also govern the reporting of payments or other transfers of value, many of which differ from each other in significant ways, are often not pre-empted, and may have a more prohibitive effect than the Sunshine Act, thus further complicating compliance efforts.

Similar federal, state and foreign fraud and abuse laws and regulations, such as state anti-kickback and false claims laws, may apply to sales or marketing arrangements and claims involving healthcare items or services. Such laws are generally broad and are enforced by various state agencies and private actions. Many U.S. states have adopted laws similar to the federal Anti-Kickback Statute and False Claims Act, and may apply to our business practices, including, but not limited to, research, distribution, sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental payors, including private insurers. In addition, some states have passed laws that require us to comply with the April 2003 Office of Inspector General Compliance Program Guidance for Pharmaceutical Manufacturers and/or the Pharmaceutical Research and Manufacturers of America's Code on Interactions with Healthcare Professionals. Additionally, we are subject to state and foreign equivalents of each of the healthcare laws and regulations described above, some of which may be broader in scope and may apply regardless of payor, in addition to items and services reimbursed under Medicaid and other state programs. Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant federal government compliance guidance, and require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures. Several states also impose other marketing restrictions or require pharmaceutical companies to make marketing or price disclosures to the state and require the registration of pharmaceutical sales representatives. State and foreign laws, including, for example, the European Union General Data Protection Regulation, which became effective May 2018 also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts. There are ambiguities as to what is required to comply with these state requirements and if we fail to comply with an applicable state law requirement we could be subject to penalties. Finally, there are state and foreign laws governing the privacy and security of health information, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

In order to distribute products commercially, we must comply with state laws that require the registration of manufacturers and wholesale distributors of drug and biological products in a state, including, in certain states, manufacturers and distributors who ship products into the state even if such manufacturers or distributors have no place of business within the state. Several states have enacted legislation requiring pharmaceutical and biotechnology companies to establish marketing compliance programs, file periodic reports with the state, make periodic public disclosures on sales, marketing, pricing, clinical trials and other activities, and/or register their sales representatives, as well as to prohibit pharmacies and other healthcare entities from providing certain physician prescribing data to pharmaceutical and biotechnology companies for use in sales and marketing, and to prohibit certain other sales and marketing practices. We must also comply with federal government price reporting laws, which require us to calculate and report complex pricing metrics in an accurate and timely manner to government programs. All of our activities are potentially subject to federal and state consumer protection and unfair competition laws.

The scope and enforcement of each of these laws is uncertain and subject to rapid change in the current environment of healthcare reform, especially in light of the lack of applicable precedent and regulations. Federal and state enforcement bodies have recently increased their scrutiny of interactions between healthcare companies and healthcare providers, which has led to a number of investigations, prosecutions, convictions and settlements in the healthcare industry. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, disgorgement, contractual damages, reputational harm, diminished profits and future earnings, individual imprisonment, exclusion of drugs from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our financial results. Further, defending against any such actions can be costly and time consuming, and may require significant financial and personnel resources. Therefore, even if we are successful in defending against any such actions that may be brought against us, our business may be impaired. If any of the physicians or other healthcare providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs. Ensuring business arrangements comply with applicable healthcare laws, as well as responding to possible investigations by government authorities, can be time- and resource-consuming and can divert a Company's attention from the business.

In the U.S., to help patients afford our approved product, we may utilize programs to assist them, including patient assistance programs and co-pay coupon programs for eligible patients. PAPs are regulated by and subject to guidance from CMS OIG. In addition, at least one insurer has directed its network pharmacies to no longer accept co-pay coupons for certain specialty drugs the insurer identified. Our co-pay coupon programs could become the target of similar insurer actions. In addition, in November 2013, the CMS issued guidance to the issuers of qualified health plans sold through the ACA's marketplaces encouraging such plans to reject patient cost-sharing support from third parties and indicating that the CMS intends to monitor the provision of such support and may take regulatory action to limit it in the future. The CMS subsequently issued a rule requiring individual market qualified health plans to accept third-party premium and cost-sharing payments from certain government-related entities. In September 2014, the OIG of the HHS issued a Special Advisory Bulletin warning manufacturers that they may be subject to sanctions under the federal anti-kickback statute and/or civil monetary penalty laws if they do not take appropriate steps to exclude Part D beneficiaries from using co-pay coupons. Accordingly, companies exclude these Part D beneficiaries from using co-pay coupons.

Current and Future Legislation

In the United States and some foreign jurisdictions, there have been, and likely will continue to be, a number of legislative and regulatory changes and proposed changes regarding the healthcare system directed at broadening the availability of healthcare, improving the quality of healthcare, and containing or lowering the cost of healthcare.

For example, in March 2010, the ACA was enacted in the United States. The ACA includes measures that have significantly changed, and are expected to continue to significantly change, the way healthcare is financed by both governmental and private insurers. Among the provisions of the ACA of greatest importance to the pharmaceutical industry are that the ACA:

- made several changes to the Medicaid Drug Rebate Program, including increasing pharmaceutical manufacturers' rebate liability by raising the minimum basic Medicaid rebate on most branded prescription drugs to 23.1% of average manufacturer price, or AMP, and adding a new rebate calculation for "line extensions" (i.e., new formulations, such as extended release formulations) of solid oral dosage forms of branded products, as well as potentially impacting their rebate liability by modifying the statutory definition of AMP.
- imposed a requirement on manufacturers of branded drugs to provide a 70% (increased pursuant to the Bipartisan Budget Act of 2018, effective as of 2019) point-of-sale discount off the negotiated price of branded drugs dispensed to Medicare Part D beneficiaries in the coverage gap (i.e., "donut hole") as a condition for a manufacturer's outpatient drugs being covered under Medicare Part D.
- extended a manufacturer's Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations.
- expanded the entities eligible for discounts under the 340B Drug Discount Program.
- established 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.
- imposed an annual, nondeductible fee on any entity that manufactures or imports certain branded prescription drugs, apportioned among these entities according to their market share in certain government healthcare programs.
- established a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research. The research conducted by the Patient-Centered Outcomes Research Institute may affect the market for certain pharmaceutical products. The ACA established the Center for Medicare and Medicaid Innovation within CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending.

Since its enactment, there have been numerous judicial, administrative, executive, and legislative challenges to certain aspects of the ACA. On June 17, 2021, the U.S. Supreme Court dismissed the most recent judicial challenge to the ACA brought by several states without specifically ruling on the constitutionality of the ACA. Prior to the Supreme Court's decision, President Biden issued an executive order to initiate a special enrollment period from February 15, 2021 through August 15, 2021 for purposes of obtaining health insurance coverage through the ACA marketplace. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. It is unclear how other healthcare reform measures of the Biden administration or other efforts, if any, to challenge, repeal or replace the ACA will impact our business. Prior to the Biden administration, on October 13, 2017, former President Trump signed an Executive Order which terminated 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 will 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, the 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 the payments were owed to them. On April 27, 2020, the United States Supreme Court 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. It is unclear what impact these rulings will have on our business.

In addition, CMS published a final rule that would give states greater flexibility as of 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 and regulatory changes have also been proposed and adopted in the United States since the ACA was enacted:

- On August 2, 2011, the U.S. Budget Control Act of 2011, among other things, included aggregate reductions of Medicare payments to providers of 2% per fiscal year. These reductions went into effect on April 1, 2013 and, due to subsequent legislative amendments to the statute, will remain in effect through 2030. Pursuant to the Coronavirus Aid, Relief, and Economic Security Act, also known as the CARES Act, as well as subsequent legislation, this 2% reduction was suspended from May 1, 2020 through March 31, 2022 due to the COVID-19 pandemic. Following the suspension, a 1% payment reduction began April 1, 2022, lasting through June 30, 2022. The 2% payment reduction resumed on July 1, 2022.
- On January 2, 2013, the U.S. American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several types of providers.
- On April 13, 2017, CMS published a final rule that gives states greater flexibility 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.
- 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 products 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 pharmaceutical manufacturer to make its drug products available to eligible patients as a result of the Right to Try Act.

- On May 23, 2019, CMS published a final rule to allow Medicare Advantage Plans the option of using step therapy for Part B drugs beginning January 1, 2020.
- On December 20, 2019, former President Trump signed into law the Further Consolidated Appropriations Act (H.R. 1865), which repealed the Cadillac tax, the health insurance provider tax, and the medical device excise tax. It is impossible to determine whether similar taxes could be instated in the future.
- On March 11, 2021, President Biden signed the American Rescue Plan Act of 2021 into law, which eliminates the statutory Medicaid drug rebate cap, currently set at 100% of a drug's average manufacturer price, for single source and innovator multiple source drugs, beginning January 1, 2024.
- In August 2022, the Inflation Reduction Act of 2022, or IRA was signed into law. The IRA includes several provisions that will impact our business to varying degrees, including provisions that reduce the out-of-pocket cap for Medicare Part D beneficiaries to $2,000 starting in 2025; impose new manufacturer financial liability on certain drugs in Medicare Part D, allow the U.S. government to negotiate Medicare Part B and Part D price caps for certain high-cost drugs and biologics without generic or biosimilar competition, require companies to pay rebates to Medicare for certain drug prices that increase faster than inflation, and delay the rebate rule that would limit the fees that pharmacy benefit managers can charge. Further under the IRA, orphan drugs are exempted from the Medicare drug price negotiation program, but only if they have one rare disease designation and for which the only approved indication is for that disease or condition. If a product receives multiple rare disease designations or has multiple approved indications, it will not qualify for the orphan drug exemption.

In addition, there have been several changes to the 340B drug pricing program, which imposes ceilings on prices that drug manufacturers can charge for medications sold to certain health care facilities. On December 27, 2018, the District Court for the District of Columbia invalidated a reimbursement formula change under the 340B drug pricing program, and CMS subsequently altered the FYs 2019 and 2018 reimbursement formula on specified covered outpatient drugs, or SCODs. The court ruled this change was not an "adjustment" which was within the Secretary's discretion to make but was instead a fundamental change in the reimbursement calculation. However, most recently, on July 31, 2020, the U.S. Court of Appeals for the District of Columbia Circuit overturned the district court's decision and found that the changes were within the Secretary's authority. On September 14, 2020, the plaintiffs-appellees filed a Petition for Rehearing En Banc (i.e., before the full court), but was denied on October 16, 2020. Plaintiffs-appellees filed a petition for a writ of certiorari at the Supreme Court on February 10, 2021. On Friday July 2, 2021, the Supreme Court granted the petition. It is unclear how these developments could affect covered hospitals who might purchase our future products and affect the rates we may charge such facilities for our approved products in the future, if any. On June 15, 2022, the Supreme Court unanimously reversed the Court of Appeals' decision, holding that HHS's 2018 and 2019 reimbursement rates for 340B hospitals were contrary to the statute and unlawful. We continue to review developments impacting the 340B program.

Additionally, there has been increasing legislative and enforcement interest in the United States with respect to drug pricing practices. Specifically, there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several U.S. Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, and review the relationship between pricing and manufacturer patient programs. At a federal level, President Biden signed an Executive Order on July 9, 2021 affirming the administration's policy to (i) support legislative reforms that would lower the prices of prescription drug and biologics, including by allowing Medicare to negotiate drug prices, by imposing inflation caps, and, by supporting the development and market entry of lower-cost generic drugs and biosimilars; and (ii) support the enactment of a public health insurance option. Among other things, the Executive Order also directs HHS to provide a report on actions to combat excessive pricing of prescription drugs, enhance the domestic drug supply chain, reduce the price that the Federal government pays for drugs, and address price gouging in the industry; and directs the FDA to work with states and Indian Tribes that propose to develop section 804 Importation Programs in accordance with the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, and the FDA's implementing regulations. FDA released such implementing regulations 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. On September 25, 2020, CMS stated drugs imported by states under this rule will not be eligible for federal rebates under Section 1927 of the Social Security Act and manufacturers would not report these drugs for "best price" or Average Manufacturer Price purposes. Since these drugs are not considered covered outpatient drugs, CMS further stated it will not publish a National Average Drug Acquisition Cost for these drugs. If implemented, importation of drugs from Canada may materially and adversely affect the price we receive for any of our product candidates. 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 would have been 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. However, on December 29, 2021 rescinded the Most Favored Nations rule.

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 court order, the removal and addition of the aforementioned safe harbors were delayed and recent legislation imposed a moratorium on implementation of the rule until January 1, 2026. This deadline was delayed to January 1, 2027 by the Bipartisan Safer Communities Act. The Inflation Reduction Act of 2022 further delayed implementation of this rule to January 1, 2032. Further, on December 31, 2020, CMS published a new rule, effective January 1, 2023, requiring manufacturers to ensure the full value of co-pay assistance is passed on to the patient or these dollars will count toward the Average Manufacturer Price and Best Price calculation of the drug. On May 21, 2021, PhRMA sued the HHS in the U.S. District Court for the District of Columbia, to stop the implementation of the rule claiming that the rule contradicts federal law surrounding Medicaid rebates. On May 17, 2022, the U.S. District Court for the District of Columbia granted PhRMA's motion for summary judgement invalidating the Medicaid Accumulator Rule. We cannot predict how the implementation of and any further changes to this rule will affect our business. Although a number of these and other proposed measures may require authorization through additional legislation to become effective, and the Biden administration may reverse or otherwise change these measures, both the Biden administration and Congress have indicated that they will continue to seek new legislative measures to control drug costs.

We expect that additional U.S. federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that the U.S. Federal Government will pay for healthcare drugs and services, which could result in reduced demand for our drug candidates or additional pricing pressures.

Individual states in the United States have also become increasingly active in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain drug access and marketing cost disclosure and transparency measures, and designed to encourage importation from other countries and bulk purchasing. Legally mandated price controls on payment amounts by third-party payors or other restrictions could harm our business, financial condition, results of operations and prospects. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. This could reduce the ultimate demand for our drugs or put pressure on our drug pricing, which could negatively affect our business, financial condition, results of operations and prospects.

We cannot predict what healthcare reform initiatives may be adopted in the future. Further federal, state and foreign legislative and regulatory developments are likely, and we expect ongoing initiatives to increase pressure on drug pricing. Such reforms could have an adverse effect on anticipated revenues from product candidates and may affect our overall financial condition and ability to develop product candidates.

Packaging and Distribution in the United States

If our products, once approved, are made available to authorized users of the Federal Supply Schedule of the General Services Administration, additional laws and requirements apply. Products must meet applicable child-resistant packaging requirements under the U.S. Poison Prevention Packaging Act. Manufacturing, sales, promotion and other activities also are potentially subject to federal and state consumer protection and unfair competition laws.

The distribution of pharmaceutical products is subject to additional requirements and regulations, including extensive record-keeping, licensing, storage and security requirements intended to prevent the unauthorized sale of pharmaceutical products.

The failure to comply with any of these laws or regulatory requirements subjects firms to possible legal or regulatory action. Depending on the circumstances, failure to meet applicable regulatory requirements can result in criminal prosecution, fines or other penalties, injunctions, exclusion from federal healthcare programs, requests for recall, seizure of products, total or partial suspension of production, denial or withdrawal of product approvals, or refusal to allow a firm to enter into supply contracts, including government contracts. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management’s attention from the operation of our business. Prohibitions or restrictions on sales or withdrawal of future products marketed by us could materially affect our business in an adverse way.

Changes in regulations, statutes or the interpretation of existing regulations could impact our business in the future by requiring, for example: (i) changes to our manufacturing arrangements; (ii) additions or modifications to product labeling; (iii) the recall or discontinuation of our potential products; or (iv) additional record-keeping requirements. If any such changes were to be imposed, they could adversely affect the operation of our business.

Other U.S. Environmental, Health and Safety Laws and Regulations

We may be 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. From time to time and in the future, our operations may involve the use of hazardous and flammable materials, including chemicals and biological materials, and may also produce hazardous waste products. Even if we contract with third parties for the disposal of these materials and waste products, we cannot completely eliminate the risk of contamination or injury resulting from these materials. In the event of contamination or injury resulting from the use or disposal of our 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.

We maintain workers’ compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees, but this insurance may not provide adequate coverage against potential liabilities. However, we do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. Current or future environmental laws and regulations may impair our research, development or production efforts. In addition, failure to comply with these laws and regulations may result in substantial fines, penalties or other sanctions.

U.S. Patent Term Extension and Marketing Exclusivity

Depending upon the timing, duration and specifics of FDA approval of a drug or biologic, some U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, commonly referred to as the Hatch-Waxman Act. The Hatch-Waxman Act permits extension of a patent term of up to five years beyond the normal expiration date of the patent as compensation for patent term lost during the FDA regulatory review process. Patent term extension, however, cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date and only those claims covering such approved drug product, a method for using it or a method for manufacturing it may be extended. Only one patent applicable to an approved drug is eligible for the extension and the application for the extension must be submitted prior to the expiration of the patent. The USPTO, in consultation with the FDA, reviews and approves the application for any patent term extension. An NDA or BLA applicant may apply for extension of patent term for its currently owned or licensed patents to add patent life beyond its current expiration date, depending on the expected length of the clinical trials and other factors involved in the filing of the relevant NDA or BLA.

Marketing exclusivity provisions under the FDCA also can delay the submission or the approval of certain applications. The FDCA provides a five-year period of non-patent marketing exclusivity within the United States to the first applicant to gain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not accept for review an ANDA, or a 505(b)(2) NDA submitted by another Company for another version of such drug where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement. The FDCA also provides three years of marketing exclusivity for an NDA, 505(b)(2) NDA or supplement to an existing NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example, new indications, dosages or strengths of an existing drug. This three-year exclusivity covers only the conditions of use associated with the new clinical investigations and does not prohibit the FDA from approving ANDAs for drugs containing the original active agent. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

European Union Drug Development

In the European Union or EU, our future products also may be subject to extensive regulatory requirements. As in the United States, medicinal products can be marketed only if a marketing authorization from the competent regulatory agencies has been obtained.

Similar to the United States, the various phases of preclinical and clinical research in the European Union are subject to significant regulatory controls.

In April 2014, the EU adopted the new Clinical Trials Regulation (EU) No 536/2014, or EU Clinical Trials Regulation, which replaced the Clinical Trials Directive 2001/20/EC, or Directive, on January 31, 2022. The transitory provisions of the new EU Clinical Trials Regulation provided that, by January 31, 2025, all ongoing clinical trials must have transitioned to the new EU Clinical Trials Regulation.

The new EU Clinical Trials Regulation overhauled the previous system of approvals for clinical trials in the EU. Specifically, the new EU Clinical Trials Regulation, which is directly applicable in all Member States (meaning no national implementing legislation in each EU Member State is required), aims at simplifying and streamlining the approval of clinical trials in the EU. For instance, it provides for a streamlined application procedure via a single entry point (through the Clinical Trials Information Systems) and strictly defined deadlines for the assessment of clinical trial applications.

European Union Drug Review and Approval

In the EU, medicinal products can only be commercialized after obtaining a marketing authorization, or MA. There are two types of marketing authorizations.

- The centralized MA is issued by the European Commission through the centralized procedure, based on the opinion of the Committee for Medicinal Products for Human Use, or CHMP, of the EMA, and is valid throughout the entire territory of the EU, and in the additional Member States of the European Economic Area (Iceland, Liechtenstein and Norway). The centralized procedure is mandatory for certain types of products, including medicines produced by biotechnological processes, products designated as orphan medicinal products, advanced-therapy medicinal products (gene-therapy, somatic cell-therapy or tissue-engineered medicines) and medicinal products containing a new active substance indicated for the treatment of HIV, AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune and other immune dysfunctions and viral diseases. The centralized procedure is optional for products containing a new active substance not yet authorized in the EU, or for products that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the EU.
- Under the centralized procedure, the EMA's Committee for Medicinal Products for Human use, or CHMP, is responsible for conducting the initial assessment of a product and for several post-authorization and maintenance activities, such as the assessment of modifications or extensions to an existing MA. Under the centralized procedure in the EU, the maximum timeframe for the evaluation of a marketing authorization application, or MAA, by the EMA is 210 days, excluding clock stops, when additional written or oral information is to be provided by the applicant in response to questions asked by the CHMP. Clock stops may extend the timeframe of evaluation of an MAA considerably beyond 210 days. Where the CHMP gives a positive opinion, it provides the opinion together with supporting documentation to the European Commission, who makes the final decision to grant an MA, which is issued within 67 days of receipt of the EMA's recommendation. Accelerated assessment might be granted by the CHMP in exceptional cases, when a medicinal product is expected to be of major public health interest, particularly from the point of view of therapeutic innovation. If the CHMP accepts such request, the time limit of 210 days will be reduced to 150 days, excluding clock stops, but it is possible that the CHMP may revert to the standard time limit for the centralized procedure if it determines that the application is no longer appropriate to conduct an accelerated assessment.
- National MAs, which are issued by the competent authorities of the Member States of the EU and only cover their respective territory, are available for products not falling within the mandatory scope of the centralized procedure. Where a product has already been authorized for marketing in a Member State of the EU, this national MA can be recognized in another Member State through the mutual recognition procedure. If the product has not received a national MA in any Member State at the time of application, it can be approved simultaneously in various Member States through the decentralized procedure. Under the decentralized procedure an identical dossier is submitted to the competent authorities of each of the Member States in which the MA is sought, one of which is selected by the applicant as the Reference Member State, or RMS. The competent authority of the RMS prepares a draft assessment report, a draft summary of the product characteristics, or SmPC, and a draft of the labeling and package leaflet, which are sent to the other Member States (referred to as the Concerned Member States) for their approval. If the Concerned Member States raise no objections, based on a potential serious risk to public health, to the assessment, SmPC, labeling, or packaging proposed by the RMS, the product is subsequently granted a national MA in all the Member States (i.e., in the RMS and the Concerned Member States).

Under the above described procedures, before granting the MA, the EMA or the competent authorities of the Member States of the EU make an assessment of the risk-benefit balance of the product on the basis of scientific criteria concerning its quality, safety and efficacy.

Now that the United Kingdom (which comprises Great Britain and Northern Ireland) has left the European Union, Great Britain is no longer covered by centralized MAs (under the Northern Ireland Protocol, centralized MAs continue to be recognized in Northern Ireland). All medicinal products with a current centralized MA were automatically converted to Great Britain MAs on January, 1 2021. For a period of three years from January 1, 2021, the Medicines and Healthcare products Regulatory Agency, or MHRA, the UK medicines regulator, may rely on a decision taken by the European Commission on the approval of a new MA in the centralized procedure, in order to more quickly grant a new Great Britain MA. A separate application will, however, still be required. On January 24, 2023, the MHRA announced that a new international recognition framework will be put in place from January 1, 2024, which will have regard to decisions on the approval of MAs made by the European Medicines Agency and certain other regulators. The MHRA also has the power to have regard to MAs approved in EU Member States through decentralized or mutual recognition procedures with a view to more quickly granting an MA in the United Kingdom or Great Britain.

European Union New Chemical Entity Exclusivity

In the EU, innovative medicinal products approved on the basis of a complete and independent data package qualify for eight years of data exclusivity upon marketing authorization and an additional two years of market exclusivity. The data exclusivity, if granted, prevents generic or biosimilar applicants from referencing the innovator’s preclinical and clinical trial data contained in the dossier of the reference product when applying for a generic or biosimilar MA in the EU, during a period of eight years from the date on which the reference product was first authorized in the EU. During the additional two-year period of market exclusivity, a generic or biosimilar MAA can be submitted, and the innovator’s data may be referenced, but no generic or biosimilar product can be placed on the EU market until the expiration of the market exclusivity. The overall ten-year period will be extended to a maximum of 11 years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are determined to bring a significant clinical benefit in comparison with currently approved therapies. There is no guarantee that a product will be considered by the EMA to be an innovative medicinal product, and products may not qualify for data exclusivity. Even if a product is considered to be an innovative medicinal product so that the innovator gains the prescribed period of data exclusivity, however, another Company could nevertheless also market another version of the product if such Company obtained an MA based on an MAA with a complete and independent data package of pharmaceutical tests, preclinical tests and clinical trials.

European Union Orphan Designation and Exclusivity

In the EU, the EMA’s Committee for Orphan Medicinal Products grants an orphan designation in respect of a product if its sponsor can establish that: (1) the product is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition; (2) either (i) such condition affects no more than five in 10,000 persons in the EU when the application is made, or (ii) it is unlikely that the product, without the benefits derived from orphan status, would generate sufficient return in the EU to justify the necessary investment in its development; and (3) there must be no satisfactory method of diagnosis, prevention or treatment of such condition authorized for marketing in the EU, or, if such a method exists, the product would be of significant benefit to those affected by that condition.

In the EU, orphan designation entitles a party to financial incentives such as reduction of fees or fee waivers and ten years of market exclusivity is granted following grant of a marketing authorization. During this market exclusivity period, neither the EMA nor the European Commission nor any of the competent authorities in the EU Members States can accept an application or grant a marketing authorization for a "similar medicinal product." A "similar medicinal product" is defined as a medicinal product containing a similar active substance or substances as contained in an authorized orphan medicinal product, and which is intended for the same therapeutic indication. This period may be reduced to six years if the orphan designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity. Market exclusivity may also be revoked in very select cases, such as if (i) it is established that a similar medicinal product is safer, more effective or otherwise clinically superior to the authorized product; (ii) the marketing authorization holder consents to such revocation; or (iii) the marketing authorization holder cannot supply enough orphan medicinal product. Orphan designation must be requested before submitting an application for marketing approval. Orphan designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

Since January 1, 2021, a separate process for orphan designation has applied in Great Britain. There is now no pre-marketing authorization orphan designation (as there is in the EU) in Great Britain and the application for orphan designation will be reviewed by the MHRA at the time of an MAA for a UK or Great Britain MA. The criteria for orphan designation are the same as in the EU, save that they apply to Great Britain only (e.g., there must be no satisfactory method of diagnosis, prevention or treatment of the condition concerned in Great Britain, as opposed to the EU).

European Pediatric Investigation Plan

In the EU, MAAs for new medicinal products have to include the results of studies conducted in the pediatric population, in compliance with a pediatric investigation plan, or PIP, agreed with the EMA's Pediatric Committee, or PDCO, unless the EMA has granted a product-specific waiver, a class waiver, or a deferral for one or more of the measures included in the PIP. This requirement also applies when a Company wants to add a new indication, pharmaceutical form or route of administration for a medicine that is already authorized. The PIP sets out the timing and measures proposed to generate data to support a pediatric indication of the drug for which marketing authorization is being sought. The PDCO can grant a deferral of the obligation to implement some or all of the measures of the PIP until there are sufficient data to demonstrate the efficacy and safety of the product in adults. Further, the obligation to provide pediatric clinical trial data can be waived by the PDCO when this data is not needed or appropriate because the product is likely to be ineffective or unsafe in children, the disease or condition for which the product is intended occurs only in adult populations, or when the product does not represent a significant therapeutic benefit over existing treatments for pediatric patients. If an MA is obtained and trial results are included in the product information, even when negative, the product is eligible for six months' supplementary protection certificate extension. In the case of orphan medicinal products, a two year extension of the orphan market exclusivity may be available. This pediatric reward is subject to specific conditions and is not automatically available when data in compliance with the PIP are developed and submitted.

Regulatory Requirements After a Marketing Authorization has been Obtained

If authorization for a medicinal product in the EU is obtained, the holder of the MA is required to comply with a range of requirements applicable to the manufacturing, marketing, promotion, and sale of medicinal products. These include:

- Compliance with the EU's stringent pharmacovigilance or safety reporting rules must be ensured. These rules can impose post-authorization studies and additional monitoring obligations.
- The manufacturing of authorized medicinal products, for which a separate manufacturer's license is mandatory, must also be conducted in strict compliance with the applicable EU laws, regulations and guidance, including Directive 2001/83/EC, Directive 2003/94/EC, Regulation (EC) No 726/2004 and the European Commission Guidelines for Good Manufacturing Practice. These requirements include compliance with EU cGMP standards when manufacturing medicinal products and active pharmaceutical ingredients, including the manufacture of active pharmaceutical ingredients outside of the EU with the intention to import the active pharmaceutical ingredients into the EU.

- Much like the Anti-Kickback Statue prohibition in the United States, the provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products is also prohibited in the European Union. The provision of benefits or advantages to induce or reward improper performance generally is governed by the national anti-bribery laws of the European Union Member States, and the Bribery Act 2010 in the UK. Infringement of these laws could result in substantial fines and imprisonment. EU Directive 2001/83/EC, which is the EU Directive governing medicinal products for human use, further provides that, where medicinal products are being promoted to persons qualified to prescribe or supply them, no gifts, pecuniary advantages or benefits in kind may be supplied, offered or promised to such persons unless they are inexpensive and relevant to the practice of medicine or pharmacy. This provision has been transposed into the Human Medicines Regulations 2012 and so remains applicable in the UK despite its departure from the EU. Payments made to physicians in certain EU Member States must be publicly disclosed. Moreover, agreements with physicians often must be the subject of prior notification and approval by the physician's employer, his or her competent professional organization and/or the regulatory authorities of the individual EU Member States. These requirements are provided in the national laws, industry codes or professional codes of conduct, applicable in the EU Member States. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

The aforementioned EU rules are generally applicable in the European Economic Area, or EEA, which consists of the EU Member States, plus Norway, Liechtenstein, and Iceland.

Brexit and the Regulatory Framework in the United Kingdom

The UK formally left the EU on January 31, 2020, and the EU and the UK have concluded a trade and cooperation agreement, or TCA, which was provisionally applicable since January 1, 2021 and has been formally applicable since May 1, 2021. The TCA includes specific provisions concerning pharmaceuticals, which include the mutual recognition of GMP, inspections of manufacturing facilities for medicinal products and GMP documents issued, but does not foresee wholesale mutual recognition of UK and EU pharmaceutical regulations. At present, Great Britain has implemented EU legislation on the marketing, promotion and sale of medicinal products through the Human Medicines Regulations 2012 (as amended) (under the Northern Ireland Protocol, the EU regulatory framework will continue to apply in Northern Ireland). Except in respect of the new EU Clinical Trials Regulation, the regulatory regime in Great Britain therefore in many ways aligns with current EU medicines regulations, however it is possible that these regimes will diverge more significantly in the future now that Great Britain's regulatory system is independent from the EU and the TCA does not provide for mutual recognition of UK and EU pharmaceutical legislation.

European Data Collection

The collection and use of personal health data in the EEA is governed by the General Data Protection Regulation, or GDPR or EU GDPR, which became effective May 25, 2018. The GDPR applies to any Company established in the EEA and to companies established outside the EEA that process personal data in connection with the offering of goods or services to data subjects in the EEA or the monitoring of the behavior of data subjects in the EEA. The GDPR enhances data protection obligations for data controllers of personal data, including stringent requirements relating to the consent of data subjects, expanded disclosures about how personal data is used, requirements to conduct privacy impact assessments for "high risk" processing, limitations on retention of personal data, mandatory data breach notification and "privacy by design" requirements, and creates direct obligations on service providers acting as data processors. The GDPR also imposes strict rules on the transfer of personal data outside of the EEA to countries that do not ensure an adequate level of protection, like the United States. Failure to comply with the requirements of the GDPR and the related national data protection laws of the EEA Member States may result in fines up to €20 million or 4% of a company's global annual revenues for the preceding financial year, whichever is higher. Moreover, the GDPR grants data subjects the right to claim material and non-material damages resulting from infringement of the GDPR. Given the breadth and depth of changes in data protection obligations, maintaining compliance with the GDPR, will require significant time, resources and expense, and we may be required to put in place additional mechanisms ensuring compliance with the new data protection rules. This may be onerous and adversely affect our business, financial condition, results of operations and prospects.

In addition, further to the United Kingdom's exit from the European Union on January 31, 2020, the GDPR ceased to apply in the United Kingdom at the end of the transition period on December 31, 2020. However, as of January 1, 2021, the United Kingdom's European Union (Withdrawal) Act 2018 incorporated the GDPR (as it existed on December 31, 2020 but subject to certain UK specific amendments) into UK law, referred to as the UK GDPR. The UK GDPR and the UK Data Protection Act 2018 set out the United Kingdom's data protection regime, which is independent from but aligned to the European Union's data protection regime. The UK Government has announced plans to reform its data protection legal framework in the Data Reform Bill, but those have been put on hold. Non-compliance with the UK GDPR may result in monetary penalties of up to £17.5 million or 4% of worldwide revenue, whichever is higher.

The UK GDPR includes restrictions on cross-border data transfers. Adequate safeguards must be implemented to enable the transfer of personal data outside of the EU or the U.K., in particular to the U.S., in compliance with EU and UK data protection laws. On June 4, 2021, the European Commission, or EC, issued new forms of standard contractual clauses for data transfers from controllers or processors in the EEA (or otherwise subject to the EU's GDPR) to controllers or processors established outside the EEA (and not subject to the EU GDPR). The new standard contractual clauses replace the standard contractual clauses that were adopted previously under the Data Protection Directive. The UK is not subject to the EC's new standard contractual clauses but has published its own version of standard clauses, referred to as "International Data Transfer Agreement" which entered into force on March 21, 2022 and enables transfers originating from the UK. Transfers made pursuant to these new mechanisms need to be assessed on a case-by-case basis to ensure the law in the recipient country provides "essentially equivalent" protections to safeguard the transferred personal data as the EEA, and businesses are required to adopt supplementary measures if such standard is not met. We will be required to implement these new safeguards when conducting restricted data transfers under the UK GDPR and doing so will require significant effort and cost.

Although the UK is regarded as a third country under the European Union's GDPR, the European Commission has now issued a decision recognizing the UK as providing adequate protection under the EU GDPR and, therefore, transfers of personal data originating in the EU to the UK remain unrestricted. Like the EU GDPR, the UK GDPR restricts personal data transfers outside the United Kingdom to countries not regarded by the United Kingdom as providing adequate protection. The UK government has confirmed that personal data transfers from the United Kingdom to the EEA remain free flowing.

Rest of the World Regulation

For other countries outside of the European Union and the United States, such as countries in Eastern Europe, Latin America or Asia, the requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. Additionally, the clinical trials must be conducted in accordance with GCP requirements and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

If we fail to comply with applicable foreign regulatory requirements, we may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

Additional Laws and Regulations Governing International Operations

If we further expand our operations outside of the United States, we must dedicate additional resources to comply with numerous laws and regulations in each jurisdiction in which we plan to operate. The Foreign Corrupt Practices Act, or FCPA, prohibits any U.S. individual or business from paying, offering, authorizing payment or offering of anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the United States to comply with certain accounting provisions requiring the company to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations.

Compliance with the FCPA is expensive and difficult, particularly in countries in which corruption is a recognized problem. In addition, the FCPA presents particular challenges in the pharmaceutical industry, because, in many countries, hospitals are operated by the government, and doctors and other hospital employees are considered foreign officials. Certain payments to hospitals in connection with clinical trials and other work have been deemed to be improper payments to government officials and have led to FCPA enforcement actions.

Various laws, regulations and executive orders also restrict the use and dissemination outside of the United States, or the sharing with certain non-U.S. nationals, of information classified for national security purposes, as well as certain products and technical data relating to those products. If we expand our presence outside of the United States, it will require us to dedicate additional resources to comply with these laws, and these laws may preclude us from developing, manufacturing, or selling certain product candidates outside of the United States, which could limit our growth potential and increase our development costs.

The failure to comply with laws governing international business practices may result in substantial civil and criminal penalties and suspension or debarment from government contracting. The U.S. Securities and Exchange Commission, or the SEC, also may suspend or bar issuers from trading securities on U.S. exchanges for violations of the FCPA's accounting provisions.

Coverage and Reimbursement

Successful commercialization of new drug products depends in part on the extent to which reimbursement for those drug products will be available from government health administration authorities, private health insurers, and other organizations. In the United States and markets in other countries, patients generally rely on third-party payors to reimburse all or part of the costs associated with their treatment. Adequate coverage and reimbursement from governmental healthcare programs, such as Medicare and Medicaid, and commercial payors is critical to new product acceptance. Our ability to successfully commercialize our product candidates will depend in part on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers and other organizations. 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. 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. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which drug products they will pay for and establish reimbursement levels. The availability and extent of reimbursement by governmental and private payors is essential for most patients to be able to afford a drug product. Sales of drug products depend substantially, both domestically and abroad, on the extent to which the costs of drugs products are paid for 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.

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 drug products. In many countries, the prices of drug products are subject to varying price control mechanisms as part of national health systems. In general, the prices of drug products under such systems are substantially lower than in the United States. Other countries allow companies to fix their own prices for drug products, but monitor and control company profits. Accordingly, in markets outside the United States, the reimbursement for drug products may be reduced compared with the United States.

There is also significant uncertainty related to the insurance coverage and reimbursement of newly approved products 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 drug products are typically made by CMS, an agency within the HHS. CMS decides whether and to what extent a new drug product will be covered and reimbursed under Medicare, and private payors tend to follow CMS to a substantial degree. However, no uniform policy of coverage and reimbursement for drug products exists among third-party payors and coverage and reimbursement levels for drug products can differ significantly from payor to payor. Factors payors consider in determining reimbursement are based on whether the product is:

- a covered benefit under its health plan;
- safe, effective and medically necessary;
- appropriate for the specific patient;
- cost-effective; and
- neither experimental nor investigational.

Third-party payors may limit coverage to specific products on an approved list or formulary, which might not include all of the FDA-approved products for a particular indication. Also, third-party payors may refuse to include a particular branded drug on their formularies or otherwise restrict patient access to a branded drug when a less costly generic equivalent or another alternative is available. 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. Third-party payors are increasingly challenging the prices charged for medical products and services, examining the medical necessity, and reviewing the cost-effectiveness of medical products and services and imposing controls to manage costs. We cannot be sure that reimbursement will be available for any product candidate that we commercialize and, if reimbursement is available, the level of reimbursement. In addition, many pharmaceutical manufacturers must calculate and report certain price reporting metrics to the government, such as average sales price, or ASP, and best price. Penalties may apply in some cases when such metrics are not submitted accurately and timely. Further, these prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs.

The Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or the MMA, established the Medicare Part D program to provide a voluntary prescription drug benefit to Medicare beneficiaries. Under Part D, Medicare beneficiaries may enroll in prescription drug plans offered by private entities that provide coverage of outpatient prescription drugs. Unlike Medicare Parts A and B, Part D coverage is not standardized. Part D prescription drug plan sponsors are not required to pay for all covered Part D drugs, and each drug plan can develop its own drug formulary that identifies which drugs it will cover and at what tier or level. While all Medicare drug plans must give at least a standard level of coverage set by Medicare, Part D prescription drug plan sponsors are not required to pay for all covered Part D drugs, and each drug plan can develop its own drug formulary that identifies which drugs it will cover and at what tier or level. However, Part D prescription drug formularies must include drugs within each therapeutic category and class of covered Part D drugs, though not necessarily all the drugs in each category or class. Any formulary used by a Part D prescription drug plan must be developed and reviewed by a pharmacy and therapeutic committee. Government payment for some of the costs of prescription drugs may increase demand for drugs for which we obtain marketing approval. Any negotiated prices for any of our future products covered by a Part D prescription drug plan will likely be lower than the prices we might otherwise obtain. Moreover, while the MMA applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own payment rates. Any reduction in payment that results from the MMA may result in a similar reduction in payments from non-governmental payors.

For a drug product 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. The required 340B discount on a given product is calculated based on the average manufacturer price, or AMP, and Medicaid rebate amounts reported by the manufacturer. As of 2010, the ACA expanded the types of entities eligible to receive discounted 340B pricing, although under the current state of the law these newly eligible entities (with the exception of children’s hospitals) will not be eligible to receive discounted 340B pricing on orphan drugs. As 340B drug pricing is determined based on AMP and Medicaid rebate data, the revisions to the Medicaid rebate formula and AMP definition described above could cause the required 340B discount to increase. The American Recovery and Reinvestment Act of 2009 provides funding for the federal government to compare the effectiveness of different treatments for the same illness.

The plan for the research was published in 2012 by the Department of HHS, the Agency for Healthcare Research and Quality and the National Institutes for Health, and periodic reports on the status of the research and related expenditures are made to Congress. Although the results of the comparative effectiveness studies are not intended to mandate coverage policies for public or private payors, it is not clear what effect, if any, the research will have on the sales of our drug candidates, if any such drug or the condition that they are intended to treat are the subject of a trial. It is also possible that comparative effectiveness research demonstrating benefits in a competitor’s drug could adversely affect the sales of our drug candidate. If third-party payors do not consider our drugs to be cost-effective compared to other available therapies, they may not cover our drugs after approval as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow us to sell our drugs on a profitable basis.

These laws, and future state and federal healthcare reform measures may be adopted in the future, any of which may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used.

Outside of the United States, the pricing of pharmaceutical products and medical devices is subject to governmental control in many countries. For example, in the European Union, pricing and reimbursement schemes vary widely from country to country. Some Member States provide that products may be marketed only after the proposed pricing has been approved. Some Member States may require the completion of additional studies that compare the cost effectiveness of a particular therapy to currently available therapies or so-called health technology assessments, in order to obtain reimbursement or pricing approval. A Member State may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. Member States may allow companies to fix their own prices for products, but monitor and control product volumes and issue guidance to physicians to limit prescriptions. Efforts to control prices and utilization of pharmaceutical products and medical devices will likely continue as countries attempt to manage healthcare expenditures. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our product candidates. Historically, products launched in the European Union do not follow price structures of the U.S. and generally prices tend to be significantly lower.

Human Capital Management

Our human capital philosophy relies on attracting and retaining team members who consistently demonstrate top performance. Our culture and our approach to talent reinforces this philosophy, including recruiting, professional development, performance management and total rewards. We have provided below additional details on some of our core human resources processes.

As of December 31, 2022, we had 392 full-time employees and four part-time employees. Of these, 297 focus on driving forward research and development programs, either directly or through our affiliates, and 99 work across our affiliates to provide strategic business development, finance and executive leadership expertise, as well as general and administrative services generally across our affiliates. We have never had a work stoppage, and none of our employees is represented by a labor organization or under any collective-bargaining arrangements. We consider our employee relations to be good.

Recruiting

In 2020, we established a talent acquisition capability to support our affiliates in hiring the right talent at the right time. Our team of experienced talent acquisition professionals works closely with hiring managers to understand the required skills and capabilities for an open role, and then supports the interview process and evaluation of candidates. We strive to hire top talent, and therefore need a high-quality recruiting process and candidate experience. We endeavor to fill every role with the most qualified candidate possible, which sometimes requires partnership with an external recruitment agency. We are consistently looking at new opportunities and avenues to recruit talented individuals to work at BridgeBio.

The talent acquisition team’s focus in 2023 is to meet the hiring needs across BridgeBio and our affiliates. We recognize that our current and potential future team members have options for employment opportunities, including with other biotech and pharma companies, research and academic institutions, government entities, and consulting and investment firms. To attract and retain top performing team members, we focus on creating an environment that allows for autonomy, professional growth and impact while also offering a competitive total rewards package.

Professional Development and Performance Management

We invest in the professional development of our team members through regular feedback and guidance, as well as targeted learning and development opportunities to meet demonstrated needs. We established a set of five core attributes that we expect every BridgeBio team member to demonstrate while performing in their roles: Patient Champion, Entrepreneurial Operator, Truth Seeker, Inspires Excellence and High-Quality Executor.

BridgeBio conducts semi-annual performance review processes for all team members to evaluate performance and provide feedback against these attributes. The feedback focuses on strengths and opportunities for improvement to enable the professional development of all team members. At the end of the year, the performance review includes self, peer, and manager feedback and also includes a formal rating and informs compensation decisions, including performance bonus, salary adjustments and promotions.

Core Values and Ethics

Millions worldwide are afflicted with genetic diseases, but small patient populations and industry reluctance to conduct early-stage development means that for many, treatments have not been forthcoming. We are committed to bridging this gap: between business case and scientific possibility, between patient and hope. This starts with our first core value: to **put patients first**. We also strive to **think independently**. Our goal is to not simply accept the ideas and opinions of others as fact, but instead to ask “why?” and “why not?” We endeavor to bring a rigorous, first-principles mindset to each problem that we take on. We encourage all of our team members to speak up when they have an idea or feedback to share, taking pride in a culture that is **radically transparent** when it comes to debating ideas. A commitment to independent thinking requires us to consider the ideas of others and to adopt them if they prove best. We strive to maintain a culture where any idea is worthy of both consideration and testing. We know that **every minute counts**. Our decentralized model strives to deliver treatments from discovery to patients as fast as humanly possible by utilizing focused teams of experts for each asset. Big decisions can be taken by people best-equipped to understand them, without wasting time on unnecessary cycles. And we **let Science speak**. Our model was designed to promote the rational assessment of our programs. Decisions about a program’s fate are driven by its performance against a set of objective criteria, giving each potential medicine’s scientific merits the last word. All employees are responsible for upholding these values and the BridgeBio Code of Business Conduct and Ethics, which forms the foundation of our policies and practices.

Total Rewards

To attract and retain top talent, we offer a competitive total rewards package. We peg total direct compensation at the upper end of market. We link a portion of every employee’s compensation to performance through a performance bonus program. To create a sense of ownership and align employee incentives with our long-term success, we offer eligible employees equity ownership in the company through stock option or restricted stock unit grants and our employee stock purchase plan. We also designed a program to incentivize affiliate-level employees to achieve specific milestones at core value-inflection points, such as IND or NDA approval.

We focus our benefits offering on areas critical to keeping our employees and their immediate families healthy and productive. We offer physical and mental health benefits to all employees who work at least 30 hours per week, on average. We have a flexible paid time off policy to empower team members to take the time they need, when they need it.

Diversity, Equity and Inclusion

We believe that a diverse, equitable and inclusive culture is critical to BridgeBio’s success. We are proud to promote unique voices within and outside our organization, and are eager to learn from others’ experiences, as we know that a diverse and inclusive workforce is a business imperative and key to our long-term success.

In 2022, our Diversity, Equity & Inclusion, or DE&I, Executive & Steering Committees continued their impactful work in carrying out the DE&I vision for BridgeBio. The DE&I sub-committees also designed and implemented point solutions to address issues that were surfaced through related focus groups and surveys. Among the many DE&I events the Committees organized and held throughout the year, we hosted a DE&I Lunch & Learn series that focused on the prominent issues impacting underrepresented minorities in healthcare clinical trials and how we, as a company, can do our part to help address these disparities.

Employee Resource Groups (ERGs) continued to be a foundational element to our DE&I efforts. The Women at Bridge ERG continued to have an impact across the Company in 2022. We built upon our speaker series and featured talks from influential women in the sciences, including members of our Board of Directors. Our mentorship program continued to drive impact as well.

The success of Women at Bridge inspired a second employee resource group to emerge, Asians@Bridge, in the third quarter of 2021. Asians@Bridge held a series of cultural, educational and community events in 2022 that received exceptional feedback from participants and attendees. We also kicked off the planning for an employee resource group supporting the LGBTQ community, called Pride@Bridge, which was launched in January 2023.

Response to COVID-19

With the continuation of the COVID-19 global pandemic, we continue to take extra precautions to reduce the risk of virus exposure for all employees, and to place our employees' health and safety front and center. Our response to the pandemic in 2022 revolved around three major components: (1) adequate safety protocols; (2) testing requirements; and (3) vaccination requirements.

- **Safety protocols:** Building off the strong framework we laid in 2020, we continued to tune our protocols in accordance with federal, including Center for Disease Control and Prevention, state, and local guidelines. Our Covid Task Force, formed in 2020, met and continues to meet regularly to ensure we are staying on top of the rapidly changing situation across all of our facilities, and communicating these changes to our employees in a timely manner.
- **Testing:** We continue to offer testing options for all BridgeBio employees who are on-site. In addition, in advance of any larger scale events, we worked to ensure that all attendees attested to having obtained a negative test prior to attendance.
- **Vaccines:** We made the decision in 2021 to mandate vaccines for all of our employees in the wake of President Biden's and the Occupational Safety and Health Administration's mandate. We created a vaccine exemption request review committee and implemented a formal process for evaluating those with either a medical or a sincerely held religious belief exemption request.

Corporate and Other Information

We were incorporated as a Delaware corporation in 2019 under the name BridgeBio Pharma, Inc. Our principal executive offices are located at 3160 Porter Drive, Suite 250, Palo Alto, CA 94304. Our telephone number is (650) 391-9740.

Our web page address is *https://bridgebio.com*. Our investor relations website is located at *https://investor.bridgebio.com*. We make available free of charge on our investor relations website under "SEC Filings" our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, including exhibits, our directors' and officers' Section 16 Reports and any amendments to those reports after filing or furnishing such materials to the SEC. References to our website address do not constitute incorporation by reference of the information contained on the website, and the information contained on the website is not part of this document or any other document that we file with or furnish to the SEC.

ITEM 1A. RISK FACTORS

Our business involves significant risks, some of which are described below. You should carefully consider the risks and uncertainties described below, together with all of the other information contained in this Annual Report on Form 10-K, including "Management's Discussion and Analysis of Financial Condition and Results of Operations" and the consolidated financial statements and the related notes. If any of the following risks actually occur, it could harm our business, prospects, operating results and financial condition and future prospects. In such event, the market price of our common stock could decline, and you could lose all or part of your investment. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also impair our business operations. This Annual Report on Form 10-K also contains forward-looking statements that involve risks and uncertainties. Our actual results could differ materially from those anticipated in the forward-looking statements as a result of factors that are described below and elsewhere in this Annual Report.

Risks Related to Our Financial Position and Growth Strategy

Drug development is a highly uncertain undertaking and involves a substantial degree of risk. We have incurred significant losses since our inception and anticipate that we will continue to incur significant losses for the foreseeable future. We have not generated significant revenue since inception, which, together with our limited operating history, may make it difficult for you to assess our future viability.

Pharmaceutical and biopharmaceutical product development is a highly speculative undertaking and involves a substantial degree of risk. We are a newly commercial-stage biopharmaceutical company with a limited operating history upon which you can evaluate our business and prospects. Our subsidiaries, on whose success we largely rely, are primarily early-stage biopharmaceutical companies. To date, we have focused principally on identifying, acquiring or in-licensing and developing our product candidates at the subsidiary level, almost all of which are in discovery, lead optimization, preclinical or clinical development. Our pipeline of product candidates will require substantial additional development time, including extensive clinical research, and resources before we would be able to apply for or receive additional regulatory approvals and begin generating revenue from sales of those product candidates, if approved.

We are not profitable and have incurred losses in each year since our inception in April 2015. Our net losses for the years ended December 31, 2022, 2021 and 2020 were $484.7 million, $586.5 million and $505.5 million, respectively. As of December 31, 2022, we had an accumulated deficit of $1.9 billion. We had two products approved for commercial sale, NULIBRY and TRUSELTIQ, but did not generate any significant revenues from product sales, and have financed operations solely through the sale of equity securities, debt financings and sale of certain assets. Sentynl purchased the global rights to NULIBRY in March 2022 and Helsinn, who is the principal selling party of TRUSELTIQ, will discontinue selling TRUSELTIQ by March 31, 2023. 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. In addition, as a result of the ongoing COVID-19 pandemic, we believe that potential delays in our ongoing and planned clinical trials and adjustments to certain of our study procedures with respect to our ongoing clinical trials, such as enabling alternate site, telehealth and home visits and at-home drug delivery, could increase our expenditures or draw out our expenditures over a longer period of time than originally estimated. Additionally, changes to our selection of contract research organizations, or CROs, for non-clinical laboratory activities and engagement with contract manufacturing organizations, or CMOs, to mitigate any potential near-term impacts to our supply chain may increase our expenditures relative to initial expectations. We anticipate these losses will increase substantially in future periods.

Because of the numerous risks and uncertainties associated with drug development and commercialization, 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 U.S. Food and Drug Administration, or FDA, or comparable foreign regulatory authorities, to conduct nonclinical or preclinical studies or clinical trials in addition to those that we currently anticipate or to otherwise provide data beyond that which we currently believe is necessary to support an application for marketing approval or to continue clinical development, or if there are any delays in any of our or our future collaborators' clinical trials or the development of our product candidates, that we may identify. We anticipate incurring significant costs associated with commercializing any future product candidates, if approved, and ongoing compliance efforts.

We may never be able to successfully commercialize a marketable drug or achieve profitability. Revenue from the sale of any product will be dependent, in part, upon the size of the markets in the territories for which we have or may gain regulatory approval, the accepted price for the product, 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. Even if we achieve profitability in the future, we may not be able to sustain profitability in subsequent periods. Our failure to achieve sustained profitability would depress the value of our Company and could impair our ability to raise capital, expand our business, diversify our research and development pipeline, market our product candidates, if approved, that we may identify and pursue, or continue our operations. Our prior losses, combined with expected future losses, have had and will continue to have an adverse effect on our stockholders' deficit and working capital.

If we obtain a controlling interest in additional companies in the future, it could adversely affect our operating results and the value of our common stock, thereby disrupting our business.

As part of our strategy, we expect to form and invest in additional wholly-owned subsidiaries and variable interest entities, or VIEs. Investments in our existing and any future subsidiaries involve numerous risks, including, but not necessarily limited to:

- risk of conducting research and development activities in new therapeutic areas or treatment modalities in which we have little to no experience;
- diversion of financial and managerial resources from existing operations;
- our ability to negotiate a proposed acquisition, in-license or investment in a timely manner or at a price or on terms and conditions favorable to us;
- our ability to combine and integrate 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 a potential 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 research and development 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. For instance, in January 2021, we completed our acquisition of all of the outstanding shares of common stock of Eidos that were not previously owned by us or our subsidiaries, to which we refer as the Eidos Merger. In connection with the Eidos Merger and our integration of Eidos' historical operations into our business, the attention of certain members of each company's management and each company's resources were diverted from day-to-day business operations. Additionally, the interests of our stockholders were diluted as a result of our issuance of shares of our common stock to Eidos' stockholders and our assumption of certain equity awards of Eidos in connection with the transaction. We may engage in similar discussions in the future with respect to other potential transactions that may divert our time and resources from our ongoing operations. In addition, from time to time we have pursued, and may in the future pursue, research and development programs through our wholly-owned subsidiaries and VIEs that we may ultimately determine not to advance, based on our ongoing assessment of the likelihood of success relative to the costs and risks associated with the program.

Risks Related to the Development of Our Product Candidates

We may encounter substantial delays in clinical trials, or may not be able to conduct or complete clinical trials on the expected timelines, if at all.

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 ongoing and future 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 product candidate development;
- delays in reaching a consensus with regulatory agencies as to the design or implementation of our clinical trials;
- delays in reaching agreement on acceptable terms with prospective 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 Investigational New Drug application, or IND, or IND amendment, clinical trial application, or CTA, or CTA amendment, or equivalent application or amendment; or 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 product candidates with the same targets or related modalities as our product candidates conducted by third parties that raise regulatory or safety concerns about risk to patients of the treatment, or if the FDA or other governmental authority 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;
- difficulty collaborating with patient groups and investigators;
- failure by CROs, other third parties or us to adhere to clinical trial requirements;
- failure 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 adverse events, or AEs, associated with the product 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 product candidates that we may identify and pursue being greater than we anticipate;

- clinical trials of any product candidates that we may identify and pursue producing negative or inconclusive results or failing to meet a specified endpoint, which may result in our deciding, or regulators requiring us, to conduct additional clinical trials or to abandon product development programs;
- delays in clinical trial enrollment or clinical trial initiation resulting from the ongoing COVID-19 pandemic, including the emergence of new variants, or any future pandemics;
- transfer of manufacturing processes to larger-scale facilities operated by a CMO, or by us, and delays or failure by our CMOs or us to make any necessary changes to such manufacturing process; and
- delays in manufacturing, testing, releasing, validating or importing/exporting sufficient stable quantities of product candidates that we may identify for use in clinical trials, or the inability to do any of the foregoing.

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 product candidates, we may be required to or we may elect to conduct additional nonclinical studies or clinical trials to bridge data obtained from our modified product candidates to data obtained from nonclinical and clinical research conducted using earlier versions of these product candidates. Clinical trial delays could also shorten any periods during which our product candidates have patent protection and may allow our competitors to bring products to market before we do, which could impair our ability to successfully commercialize product candidates and may harm our business and results of operations.

We could also encounter delays if an ongoing or planned clinical trial is suspended or terminated by us, by the data safety monitoring board, or DSMB, including for our ongoing Phase 3 clinical trial of acoramidis, ongoing Phase 2 and planned Phase 3 clinical trials of low-dose infigratinib, our ongoing Phase 2 and planned Phase 3 clinical trials of BBP-418, our ongoing Phase 1/2 clinical trial of BBP-631 and our ongoing Phase 2b and Phase 3 clinical trials of encaleret, or by the FDA or other regulatory authority, 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 or other 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 product candidate, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. For instance, although acoramidis failed to meet its primary endpoint at Month 12 in the ATTRibute-CM Study, the ATTRibute-CM independent data monitoring committee recommended continuing the study through the Month 30 endpoint based on unblinded data reviews. We have in the past received, and may receive in the future, partial or full clinical hold notices from the FDA or other regulatory authorities, which have required, and may in the future require, us to conduct additional studies, generate additional data, amend our clinical trial protocols and/or delay or halt the initiation or continuation of our clinical trials. We may be required or may voluntarily determine to place one or more of our product candidates on clinical hold in the future for various reasons, which could delay or otherwise impair our clinical development efforts and ability to obtain regulatory approval for any such product candidate. Additionally, the FDA may determine, upon review of an IND submission, that we have not provided sufficient information needed to assess the risks to subjects of the proposed studies, or that our IND submission is otherwise insufficient to support initiation of a clinical trial. There is no guarantee that the FDA will agree that our responses are sufficient, and we may be required to conduct additional preclinical studies or manufacturing steps before the FDA allows our proposed clinical trials to proceed.

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 or comparable foreign regulatory authorities. The FDA 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 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 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 product candidates.

Delays in the initiation, conduct or completion of any clinical trial of our product candidates will increase our costs, slow down the product candidate development and approval process and delay or potentially jeopardize our ability to commence product sales and generate revenue from such product candidates, if approved. 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 our product candidates. In the event we identify any additional product candidates to pursue, we cannot be sure that submission of an IND or a CTA will result in the FDA 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.

Results of earlier studies or clinical trials may not be predictive of future clinical trial results, and initial studies or clinical trials may not establish an adequate safety or efficacy profile for our product candidates to justify proceeding to advanced clinical trials or an application for regulatory approval.

The results of nonclinical and preclinical studies and clinical trials may not be predictive of the results of later-stage clinical trials, and interim results of a clinical trial do not necessarily predict final results. In addition, for certain of our product candidates that we acquired, we did not undertake the preclinical studies and clinical trials ourselves. 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 product 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 product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy profile despite having progressed through nonclinical studies and initial clinical trials. For instance, acoramidis failed to meet its primary endpoint at Month 12 in the ATTRibute-CM Study as mean observed six-minute walk distance, or 6MWD, decline for the acoramidis and placebo arms were 9 meters and 7 meters, respectively, both of which declines are similar to healthy elderly adults and less than prior untreated ATTR-CM cohorts; however, the ATTRibute-CM independent data monitoring committee has recommended that the study continue through the Month 30 endpoint based on unblinded data reviews. A number of companies in the pharmaceutical and biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier studies, and we cannot be certain that we will not face similar setbacks. Even if early-stage clinical trials are successful, we may need to conduct additional clinical trials of our product candidates in additional patient populations or under different treatment conditions before we are able to seek approvals from the FDA and regulatory authorities outside the United States to market and sell these product candidates. Our failure to obtain marketing approval for our product candidates for commercially viable indications, or at all, would substantially harm our business, prospects, financial condition and results of operations.

Additionally, some clinical trials of our product candidates performed to date were designed as open-label studies and were conducted at a limited number of clinical sites on a limited number of patients. An "open-label" clinical trial is one where both the patient and investigator know whether the patient is receiving the investigational product candidate or either an existing approved drug or placebo. Most typically, open-label clinical trials test only the investigational product candidate and sometimes may do so at different dose levels. Open-label clinical trials are subject to various limitations that may exaggerate any therapeutic effect as patients in open-label clinical trials are aware when they are receiving treatment. Open-label clinical 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. Moreover, patients selected for early clinical trials often include the most severe sufferers and their symptoms may have been bound to improve notwithstanding the new treatment. In addition, open-label clinical 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. Given that our Phase 2 clinical trial of acoramidis included an open-label clinical trial extension and our Phase 2 dose-escalation and expansion study of low-dose infigratinib in children with achondroplasia, or PROPEL 2, is designed as an open-label trial, the results from these clinical trials may not be predictive of future clinical trial results with these or other product candidates for which we include an open-label clinical trial when studied in a controlled environment with a placebo or active control.

We may encounter difficulties enrolling patients in clinical trials, and clinical development activities could thereby be delayed or otherwise adversely affected.

The timely completion of clinical trials in accordance with their protocols depends, among other things, on our ability to enroll a sufficient number of patients who remain in the trial until its conclusion. The indications for which we plan to evaluate our current product candidates represent a rare disease or condition with limited patient populations from which to draw participants in clinical trials. Due to our focus on the development of product candidates for the treatment of Mendelian diseases and genetically driven cancers, many of which are rare conditions, we may not be able to identify and enroll a sufficient number of patients, or those with required or desired characteristics and criteria, in a timely manner.

We may experience difficulties in patient enrollment in our clinical trials for a variety of reasons, 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 design of the trial;
- the ability to recruit clinical trial investigators with the appropriate competencies and experience;
- the approval or concurrent enrollment of clinical trials involving competing product candidates currently under development for Mendelian diseases or genetically driven cancers, or competing clinical trials for similar therapies or targeting patient populations meeting our patient eligibility criteria;
- clinicians' and patients' perceptions as to the potential advantages and side effects of the product candidate being studied in relation to other available therapies and product 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, including due to the ongoing COVID-19 pandemic.

If we have difficulty enrolling sufficient numbers of patients to conduct clinical trials as planned, we may need to delay or terminate ongoing or planned clinical trials, either of which would have an adverse effect on our business.

Use of our product candidates could be associated with side effects, adverse events or other properties or safety risks, which could delay or halt their clinical development, prevent their regulatory approval, cause us to suspend or discontinue clinical trials, abandon a product or product candidate, limit the commercial potential of a product candidate, if 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 adverse events, or AEs, associated with use of our product candidates. Results of our clinical trials could reveal a high and unacceptable severity and prevalence of side effects or unexpected characteristics. Undesirable side effects caused by our product candidates could cause us or regulatory authorities to interrupt, delay or halt clinical trials, and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or comparable foreign regulatory authorities. The drug-related side effects of our product candidates 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 our product candidates 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 product 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. For instance, in our Phase 2 clinical trial of infigratinib for the treatment of FGFR-driven cancers, the most commonly reported treatment emergent AE of any grade was hyperphosphatemia, which is an electrolyte disorder in which there is an elevated level of phosphate in the blood. These and other AEs that we may observe in our ongoing and future preclinical studies and clinical trials of our product candidates could require us to delay, modify or abandon our development plans for the affected product candidate or other product candidates that share properties of the affected product candidate. Many product 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 product candidates and to identify new product candidates, we cannot be certain that later testing or trials of product 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 our product candidates in larger, longer and more extensive clinical trials, or as the use of our product candidates, if they receive regulatory approval, becomes more widespread, 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, such findings may harm our business, financial condition and prospects significantly.

Additionally, adverse developments in clinical trials of pharmaceutical and biopharmaceutical products conducted by others may cause the FDA or other regulatory oversight bodies to suspend or terminate our clinical trials, to change the requirements for approval of any of our product candidates.

In addition to side effects caused by a product candidate, the administration process or related procedures also can cause adverse side effects. If any such AEs occur, our clinical trials of a product candidate could be suspended or terminated. If we are unable to demonstrate that any AEs were caused by the administration process or related procedures, the FDA, the European Commission, the EMA, or other regulatory authorities could order us to cease further development of, or deny approval of, a product candidate for any or all targeted indications. Even if we can demonstrate that all future serious adverse events, or SAEs, are not product-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 product candidates, the commercial prospects of such product candidates may be harmed and our ability to generate product revenues from any of these product candidates may be delayed or eliminated. Any of these occurrences may harm our ability to develop other product candidates, and may harm our business, financial condition and prospects significantly.

Additionally, if any of our product candidates receives marketing approval, the FDA could impose a boxed warning in the labeling of our product and 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 product outweigh its risks, which may include, among other things, a Medication Guide outlining the risks of the product for distribution to patients and a communication plan to health care practitioners. Furthermore, if we or others later identify undesirable side effects caused by our product candidates once approved, several potentially significant negative consequences could result, including:

- regulatory authorities may suspend or withdraw approvals of such product or product candidate;
- regulatory authorities may require additional warnings or statements on the label;
- regulatory authorities may refuse to approve label expansion for additional indications of such product or product candidate;
- we may be required by the FDA to implement a REMS;
- we may be required to change the way a product or product candidate is distributed, administered or conduct additional clinical trials;
- we may be subject to regulatory investigations and enforcement actions;
- we may decide to remove such product or product candidate from the marketplace;
- 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 product or product candidate, if approved, and may harm our business, financial condition and prospects significantly.

Certain of our product candidates are under development for the treatment of patient populations with significant comorbidities that may result in deaths or serious adverse or unacceptable side effects and require us to abandon or limit our clinical development activities.

Patients in certain of our ongoing and planned clinical trials of product candidates in genetically driven cancers, including clinical trials of infigratinib of FGFR-driven cancers and our Phase 1 monotherapy dose escalation and expansion clinical trial of BBP-398 in patients with RAS and RTK mutations, as well as patients who may undergo treatment with other product candidates that we may develop, may also receive chemotherapy, radiation, and/or other high dose or myeloablative treatments in the course of treatment of their disease, and may therefore experience side effects or AEs, including death, that are unrelated to our product candidates. While these side effects or AEs may be unrelated to our product candidates, they may still affect the success of our clinical trials. The inclusion of critically ill patients in our clinical trials may also result in deaths or other adverse medical events due to underlying disease or to other therapies or medications that such patients may receive. Any of these events could prevent us from advancing our product candidates through clinical development, and from obtaining regulatory approval, and would impair our ability to commercialize our product candidates. Any inability to advance our product candidates through clinical development may harm our business, financial condition, results of operations and prospects.

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 trials. Interim data from 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 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, financial condition, results of operations and prospects.

Risks Related to Regulatory Review and Approval of our Product Candidates

Our product 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 product candidates will receive regulatory approval, which is necessary before they can be commercialized.

Before obtaining marketing approval from regulatory authorities for the sale of our product candidates, we must conduct extensive clinical trials to demonstrate the safety and efficacy of the product candidates in humans. To date, we have focused substantially all of our efforts and financial resources on identifying, acquiring, and developing our product candidates, including conducting lead optimization, nonclinical studies, preclinical studies and clinical trials, and providing general and administrative support for these operations. We cannot be certain that any clinical trials will be conducted as planned or completed on schedule, if at all. Our 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 ability to successfully develop, obtain regulatory approval for, and then successfully commercialize product candidates. While we previously had two products approved for sale, we have not generated significant revenue from sales of drugs, and we may never be able to successfully commercialize a marketable drug.

All of our product candidates require additional development; management of preclinical, clinical and manufacturing activities; and regulatory approval. In addition, we will need to obtain adequate manufacturing supply; complete the build-out of a commercial organization; commence product candidate-specific marketing efforts; and obtain reimbursement before we generate any significant revenue from commercial product sales from such product candidates, if ever. Many of our product 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 our product candidates will be successful in clinical trials or receive regulatory approval. Further, our product candidates may not receive regulatory approval even if they are successful in clinical trials. If we do not receive regulatory approvals for our product candidates, we and our subsidiaries may not be able to continue operations, which may result in us winding down and dissolving the subsidiary, selling or out-licensing the technology or pursuing an alternative strategy.

If we are unable to obtain regulatory approval in one or more jurisdictions for any product candidates that we may identify and develop, our business will be substantially harmed.

We cannot commercialize a product until the appropriate regulatory authorities have reviewed and approved the product candidate. Approval by the FDA and comparable foreign regulatory authorities is lengthy and unpredictable, and depends upon numerous factors, including substantial discretion of the regulatory authorities. Approval policies, regulations or the type and amount of nonclinical or clinical data necessary to gain approval may change during the course of a product candidate's development and may vary among jurisdictions, which may cause delays in the approval or the decision not to approve an application. While we previously obtained regulatory approvals from the FDA, European Medicines Agency, or EMA, and State of Israel Ministry of Health, for NULIBRY (fosdenopterin) to reduce the risk of mortality in patients with molybdenum cofactor deficiency, or MoCD, Type A, and from the FDA and Health Canada for TRUSELTIQ (infigratinib) for the treatment of adults with previously treated, unresectable locally advanced or metastatic cholangiocarcinoma with a FGFR2 fusion or other rearrangement, it is possible that our current product candidates and any other product candidates which we may seek to develop in the future will not ever obtain regulatory approval. We cannot be certain that any of our product candidates will receive regulatory approval or that if approved, any of our product candidates, will be successfully commercialized.

Obtaining marketing approval is an extensive, lengthy, expensive and inherently uncertain process, and regulatory authorities may delay, limit or deny approval of our product candidates for many reasons, including, but not limited to:

- the inability to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that the applicable product candidate is safe and effective as a treatment for our targeted indications;
- the FDA or comparable foreign regulatory authorities may disagree with the design, endpoints or implementation of our 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 seek approval;
- the FDA or comparable foreign regulatory authorities may require additional preclinical studies or clinical trials beyond those that we currently anticipate;
- the FDA or comparable foreign regulatory authorities may disagree with our interpretation of data from nonclinical studies or clinical trials;
- the data collected from clinical trials of product candidates that we may identify and pursue may not be sufficient to support the submission of a new drug application, or NDA, biologics license application, or BLA, or other submission for regulatory approval in the United States or elsewhere;
- we may be unable to demonstrate to the FDA or comparable foreign regulatory authorities that a product candidate's risk-benefit ratio for its proposed indication is acceptable;
- the FDA 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 contract for clinical and commercial supplies; and
- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may change in a manner that renders the clinical trial design or data insufficient for approval.

In addition, even if an NDA, BLA, or other submission for regulatory approval, is filed and accepted for review, the FDA or comparable regulatory authorities may delay their review or approval process or may decline to grant regulatory approval for a variety of reasons. The lengthy approval process, as well as the unpredictability of the results of clinical trials and evolving regulatory requirements, may result in our failure to obtain regulatory approval to market product candidates that we may pursue in the United States or elsewhere, which would significantly harm our business, prospects, financial condition and results of operations.

Our clinical trials may fail to demonstrate substantial evidence of the safety and efficacy of product candidates that we may identify and pursue for their intended uses, which would prevent, delay or limit the scope of regulatory approval and commercialization.

Before obtaining regulatory approvals for the commercial sale of our product candidates, we must demonstrate through lengthy, complex and expensive nonclinical studies, preclinical studies and clinical trials that the applicable product candidate is both safe and effective for use in each target indication, and in the case of our product candidates regulated as biological products, that the product candidate is safe, pure, and potent for use in its targeted indication. Each product candidate must demonstrate an adequate risk versus benefit profile in its intended patient population and 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 product candidates that begin clinical trials are never approved by regulatory authorities for commercialization. We have limited experience in designing clinical trials and may be unable to design and execute a clinical trial to support future marketing approvals.

We cannot be certain that our current clinical trials or any other future 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 approval of our product 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 or comparable foreign regulatory authorities will interpret the results as we do, and more trials could be required before we submit our product candidates for approval. Success in clinical trials in a particular indication does not ensure that a product candidate will be successful in other indications. Similarly, approval of a product candidate in a particular indication does not ensure that that the product candidate will be successful in other indications. 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 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 product candidates. Even if regulatory approval is secured for a product candidate, the terms of such approval may limit the scope and use of the specific product candidate, which may also limit its commercial potential.

We conduct clinical trials for product candidates outside the United States, and the FDA and comparable foreign regulatory authorities may not accept data from such trials.

We currently conduct clinical trials outside the United States, including in Europe. For instance, our Phase 3 clinical trials of acoramidis include patients outside of the United States. The acceptance by the FDA or comparable foreign regulatory authority of study data from clinical trials conducted outside the United States or another jurisdiction may be subject to certain conditions or may not be accepted at all. In cases where data from foreign clinical trials are intended to serve as the basis for marketing approval 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) the data may be considered valid without the need for an on-site inspection by the FDA or, if the FDA considers such as inspection to be necessary, the FDA is able to validate the data through an on-site inspection or other appropriate means. Additionally, the FDA's clinical trial requirements, including sufficient size of patient populations and statistical powering, must be met. 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 or any comparable foreign regulatory authority will accept data from trials conducted outside of the United States or the applicable jurisdiction, including from our ongoing and planned Phase 3 clinical trials of acoramidis, for which we have enrolled cohorts outside the United States. If the FDA 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 product candidates that we may develop not receiving approval or clearance for commercialization in the applicable jurisdiction.

Even if we obtain FDA approval for our current product candidates in the United States, we may never obtain approval to commercialize any of these product candidates outside of the United States, which would limit our ability to realize their full market potential.

In order to market any products outside of the United States, we 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 product 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 product 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 products, once approved is also subject to approval.

Seeking foreign regulatory approval could result in difficulties and costs and require additional nonclinical 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 product candidates in those countries. The foreign regulatory approval process may include all of the risks associated with obtaining FDA approval. While we previously had two products approved for sale in the United States, we do not have any product candidates approved for sale in international markets, and we do not have experience in obtaining regulatory approval in international markets. If we fail to comply with regulatory requirements in international markets or to obtain and maintain required approvals, or if regulatory approval in international markets is delayed, our target market will be reduced and our ability to realize the full market potential of any approved products will be harmed.

Even though we may apply for orphan drug designation for our product candidates, we may not be able to obtain such designations or maintain the benefits associated with orphan drug status, including orphan drug marketing exclusivity.

Our business strategy focuses on the development of product candidates for the treatment of genetic diseases, which may be eligible for FDA or EMA orphan drug designation. Regulatory authorities in some jurisdictions, including the United States and European Union, may designate drugs or biologics 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 annually in the United States, or a patient population of 200,000 or more in the United States where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the United States. In order to obtain orphan drug designation, the request must be made before submitting an NDA or BLA. In the United States, orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages, and user-fee waivers. After the FDA grants orphan drug designation, the generic identity of the drug and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process

If a product that has orphan drug designation subsequently receives the first FDA approval of that particular product for the disease for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications, including an NDA or BLA, to market the same drug or biologic for the same indication for seven years, except in limited circumstances such as a showing of clinical superiority to the product with orphan drug exclusivity or if the FDA finds that the holder of the orphan drug exclusivity has not shown that it can assure the availability of sufficient quantities of the orphan drug to meet the needs of patients with the disease or condition for which the drug was designated. As a result, even if one of our product candidates receives orphan exclusivity, the FDA can still approve other drugs or biologics for use in treating the same indication or disease or the same biologic for a different indication or disease during the exclusivity period. Furthermore, the FDA can waive orphan exclusivity if we are unable to manufacture sufficient supply of our product or orphan drug exclusivity can be overcome if a subsequent applicant demonstrates clinical superiority over our product.

In the European Union, the Committee for Orphan Medicinal Products of the EMA grants an orphan designation in respect of a product if its sponsor can establish that (1) the product is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition, (2) either (i) such condition affects not more than five in 10,000 persons in the European Union when the application is made, or (ii) it is unlikely that the product, without the benefits derived from orphan status, would generate sufficient return in the European Union to justify the necessary investment in its development; and (3) there must be no satisfactory method of diagnosis, prevention, or treatment of such condition authorized for marketing in the European Union, or, if such method exists, the product would be of significant benefit to those affected by that condition.

We have obtained from the FDA orphan drug designations, including for: acoramidis for the treatment of transthyretin amyloidosis; low-dose infigratinib for the treatment of achondroplasia; encaleret for the treatment of autosomal dominant hypocalcemia (including ADH type 1 and ADH type 2); BBP-631 for the treatment of CAH caused by 21OHD; BBP-812 for the treatment of Canavan Disease; and BBP-671 for the treatment of PKAN and PA. We have obtained from the EMA and European Commission, orphan drug designation for: acoramidis for the treatment of ATTR amyloidosis; low-dose infigratinib for the treatment of achondroplasia; BBP-631 for the treatment of CAH caused by 21 OHD; BBP-418 for the treatment of limb-girdle muscular dystrophy; BBP-812 for the treatment of Canavan Disease; BBP-671 for the treatment of PKAN and PA; and encaleret as a treatment for hypoparathyroidism (inclusive of ADH1). We may seek orphan drug designation for other product candidates. Even if we obtain orphan drug designation, exclusive marketing rights in the United States may be limited if we seek approval for an indication broader than the orphan designated indication and may be lost if the FDA later determines that the request for designation was materially defective, if we are unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition, or if a subsequent applicant demonstrates clinical superiority over our products. In addition, although we may seek orphan drug designation for other product candidates, we may never receive such designations. Any failure to obtain, maintain or otherwise recognize the benefits of orphan drug designation for our product candidates could have a material adverse effect on our prospects.

On August 3, 2017, Congress passed the FDA Reauthorization Act of 2017, or FDARA. FDARA, among other things, codified the FDA's pre-existing regulatory interpretation to require that a sponsor demonstrate the clinical superiority of an orphan drug that is otherwise the same as a previously approved drug for the same rare disease in order to receive orphan drug exclusivity. The legislation reverses prior precedent holding that the Orphan Drug Act unambiguously requires that the FDA recognize the orphan exclusivity period regardless of a showing of clinical superiority. Moreover, in the Consolidated Appropriations Act of 2021, Congress did not further change this interpretation when it clarified that the interpretation codified in FDARA would apply in cases where FDA issued an orphan designation before the enactment of FDARA but where product approval came after the enactment of FDARA. The FDA may further reevaluate the Orphan Drug Act and its regulations and policies. We do not know if, when, or how the FDA may change the orphan drug regulations and policies in the future, and it is uncertain how any changes might affect our business. Depending on what changes the FDA may make to its orphan drug regulations and policies, our business could be adversely impacted.

The FDA has granted rare pediatric disease designation to BBP-671 for the treatment of PKAN and PA, low-dose infigratinib for the treatment of achondroplasia, and BBP-812 for the treatment of Canavan Disease. However, a marketing application for BBP-671, if approved, may not meet the eligibility criteria for a priority review voucher.

The FDA has granted rare pediatric disease designation to BBP-671 for the treatment of PKAN and PA, low-dose infigratinib for the treatment of achondroplasia, and BBP-812 for the treatment of Canavan Disease. Designation of a drug as a drug for a rare pediatric disease does not guarantee that an NDA for such drug will meet the eligibility criteria for a rare pediatric disease priority review voucher at the time the application is approved. Under the Federal Food, Drugs, and Cosmetic Act, or FDCA, we will need to request a rare pediatric disease priority review voucher in our original NDA for BBP-671. The FDA may determine that an NDA for any of BBP-671, low-dose infigratinib, or BBP-812, if approved, does not meet the eligibility criteria for a priority review voucher, including for the following reasons:

- achondroplasia, Canavan Disease, PKAN or PA no longer meets the definition of a rare pediatric disease;
- the NDA contains an active ingredient (including any ester or salt of the active ingredient) that has been previously approved in an NDA;
- the NDA is not deemed eligible for priority review;
- the NDA does not rely on clinical data derived from studies examining a pediatric population and dosages of the drug intended for that population (that is, if the NDA does not contain sufficient clinical data to allow for adequate labeling for use by the full range of affected pediatric patients); or
- the NDA is approved for a different adult indication than the rare pediatric disease for which BBP-671, low-dose infigratinib, or BBP-812 is designated (for example, if BBP-671, is approved for an indication based on specific genetic alterations that would be inclusive of, but not limited to, BBP-671).

The authority for the FDA to award rare pediatric disease priority review vouchers for drugs and biologics that receive rare pediatric disease designation on or prior to September 30, 2024 is currently limited to those candidates that receive rare pediatric disease designation on or prior to September 30, 2024, and the FDA may only award rare pediatric disease priority review vouchers through September 30, 2026. However, it is possible the FDA's authority to award rare pediatric disease priority review vouchers will be further extended by Congress. Absent any such extension, if an NDA for BBP-671, low-dose infigratinib or BBP-812 is not approved prior to September 30, 2026 for any reason, regardless of whether it meets the criteria for a rare pediatric disease priority review voucher, it will not be eligible for a priority review voucher.

Accelerated approval by the FDA, even if granted for any of our product candidates, may not lead to a faster development or regulatory review or approval process and it does not increase the likelihood that our product candidates will receive marketing approval.

We may seek approval of our product candidates using the FDA's accelerated approval pathway. We may seek approval of additional product candidates, where applicable, under the FDA's accelerated approval pathway. This pathway may not lead to a faster development, regulatory review or approval process and does not increase the likelihood that our product candidates will receive marketing approval. A product may be eligible for accelerated approval if it treats a serious or life-threatening condition, generally provides a meaningful advantage over available therapies, and demonstrates an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit. As a condition of approval, the FDA may require that a sponsor of a product receiving accelerated approval perform adequate and well-controlled post-marketing confirmatory clinical trials. These confirmatory trials must be completed with due diligence. Under the Food and Drug Omnibus Reform Act of 2022, or FDORA, the FDA is permitted to require, as appropriate, that a post-approval confirmatory trial or trials be underway prior to approval or within a specified time period after the date accelerated approval was granted. FDORA also requires sponsors to send updates to the FDA every 180 days on the status of such studies, including progress toward enrollment targets, and the FDA must promptly post this information publicly. Furthermore, under FDORA, the FDA is empowered to take action, such as issuing fines, against companies that fail to conduct with due diligence any post-approval confirmatory trial or submit timely reports to the agency on their progress. In addition, for products under consideration for accelerated approval, the FDA currently requires, unless otherwise requested by the agency, pre-approval of promotional materials intended for dissemination or publication within 120 days of marketing approval be submitted to the agency for review during the review period, which could adversely impact the timing of the commercial launch of the product. Thus, even if we seek to utilize the accelerated approval pathway, we may not be able to obtain accelerated approval and, even if we do, we may not experience a faster development, regulatory review or approval process for that product. In addition, receiving accelerated approval does not assure that the product's accelerated approval will eventually be converted to a traditional approval.

We may not elect or be able to take advantage of any expedited development or regulatory review and approval processes available to product candidates granted breakthrough therapy, fast track or regenerative medicine advanced therapy designation by the FDA.

We intend to evaluate and continue ongoing discussions with the FDA on regulatory strategies that could enable us to take advantage of expedited development pathways for certain of our product candidates, although we cannot be certain that our product candidates will qualify for any expedited development pathways or that regulatory authorities will grant, or allow us to maintain, the relevant qualifying designations. Potential expedited development pathways that we could pursue include breakthrough therapy, fast track designation and/or regenerative medicine advanced therapy, or RMAT.

Breakthrough therapy designation is intended to expedite the development and review of product candidates that are designed to treat serious or life-threatening diseases when "preliminary clinical evidence indicates that the drug 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 product candidate as a breakthrough therapy provides potential benefits that include more frequent meetings with the FDA to discuss the development plan for the product candidate and ensure collection of appropriate data needed to support approval; more frequent written correspondence from the FDA about matters such 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.

Fast track designation is designed for product candidates intended for the treatment of a serious or life-threatening disease or condition, where nonclinical or clinical data demonstrate the potential to address an unmet medical need for this disease or condition.

We may seek RMAT designation for one or more of our product candidates. In 2017, the FDA established the RMAT designation as part of its implementation of the 21st Century Cures Act to expedite review of any drug that meets the following criteria: it qualifies as a RMAT, which is defined as a cell therapy, therapeutic tissue engineering product, human cell and tissue product, or any combination product using such therapies or products, with limited exceptions; it is intended to treat, modify, reverse, or cure a serious or life-threatening disease or condition; and preliminary clinical evidence indicates that the drug has the potential to address unmet medical needs for such a disease or condition. Like breakthrough therapy designation, RMAT designation provides potential benefits that include more frequent meetings with the FDA to discuss the development plan for the product candidate, and eligibility for rolling review and priority review. Products granted RMAT designation may also be eligible for accelerated approval on the basis of a surrogate or intermediate endpoint reasonably likely to predict long-term clinical benefit, or reliance upon data obtained from a meaningful number of sites, including through expansion to additional sites. RMAT-designated products that receive accelerated approval may, as appropriate, fulfill their post-approval requirements through the submission of clinical evidence, clinical trials, patient registries, or other sources of real world evidence, such as electronic health records; through the collection of larger confirmatory data sets; or via post-approval monitoring of all patients treated with such therapy prior to approval of the therapy.

Although some of our product candidates, including the following, were granted fast track designation by the FDA, we may elect not to pursue any of breakthrough therapy, fast track or RMAT designations for our other product candidates, and the FDA has broad discretion whether or not to grant these designations:

- BBP-418 for the treatment of LGMD2I,
- encaleret for the treatment of ADH1,
- BBP-631 for the treatment of CA, and
- BBP-812 for the treatment of Canavan Disease.

Even if we believe a particular product candidate is eligible for breakthrough therapy, fast track designation or RMAT, there can be no assurance that the FDA would decide to grant it. Breakthrough therapy designation, fast track and RMAT designation do not change the standards for product approval, and there is no assurance that such designation or eligibility will result in expedited review or approval or that the approved indication will not be narrower than the indication covered by the breakthrough therapy, fast track or RMAT designation. Thus, even if we do receive breakthrough therapy, fast track or RMAT designation, we may not experience a faster development process, review or approval compared to conventional FDA procedures. The FDA may withdraw breakthrough therapy, fast track or RMAT designation if it believes that the product 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.

Additionally, certain oncology product candidates may be eligible for review under the Real-Time Oncology Review, or RTOR, pilot program, which is an initiative of the FDA's Oncology Center of Excellence designed to expedite the delivery of safe and effective cancer treatments to patients. Although this program allows the FDA to review data earlier, before an applicant formally submits a complete application, acceptance into the RTOR pilot does not guarantee or influence approvability of the application, which is subject to the usual benefit-risk evaluation by FDA reviewers, and it does not affect the FDA's PDUFA timelines.

We may seek designation for our platform technology as a designated platform technology, but we might not receive such designation, and even if we do, such designation may not lead to a faster development or regulatory review or approval process.

We may seek designation for our platform technology as a designated platform technology. Under FDORA, a platform technology incorporated within or utilized by a drug or biologic is eligible for designation as a designated platform technology if (1) the platform technology is incorporated in, or utilized by, a drug approved under an NDA or BLA; (2) preliminary evidence submitted by the sponsor of the approved or licensed drug, or a sponsor that has been granted a right of reference to data submitted in the application for such drug, demonstrates that the platform technology has the potential to be incorporated in, or utilized by, more than one drug without an adverse effect on quality, manufacturing, or safety; and (3) data or information submitted by the applicable person indicates that incorporation or utilization of the platform technology has a reasonable likelihood to bring significant efficiencies to the drug development or manufacturing process and to the review process. A sponsor may request the FDA to designate a platform technology as a designated platform technology concurrently with, or at any time after, submission of an IND application for a drug that incorporates or utilizes the platform technology that is the subject of the request. If so designated, the FDA may expedite the development and review of any subsequent original NDA or BLA for a drug that uses or incorporates the platform technology. Even if we believe our platform technology meets the criteria for such designation, the FDA may disagree and instead determine not to grant such designation. In addition, the receipt of such designation for a platform technology does not ensure that a drug will be developed more quickly or receive a faster FDA review process or ultimate FDA approval. Moreover, the FDA may revoke a designation if the FDA determines that a designated platform technology no longer meets the criteria for such designation.

If we are unable to successfully validate, develop and obtain regulatory approval for companion diagnostic tests for our drug candidates that require or would commercially benefit from such tests, or experience significant delays in doing so, we may not realize the full commercial potential of these product candidates.

In connection with the clinical development of our product candidates for certain indications, we 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 developed a companion diagnostic for infigratinib in patients with CCA in collaboration with Foundation Medicine, or FMI, which received FDA approval at the same time as TRUSELTIQ. Such companion diagnostics would be used during our clinical trials as well as in connection with the commercialization of our product candidates. To be successful, we or our collaborators will need to address a number of scientific, technical, regulatory and logistical challenges. The FDA 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 may develop, which we expect will require separate regulatory clearance or approval prior to commercialization.

We may rely on third parties for the design, development and manufacture of companion diagnostic tests for our therapeutic product candidates that may require such tests. If we 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 approval processes. Moreover, even if data from preclinical studies and early clinical trials appear to support development of a companion diagnostic for a product candidate, data generated in later clinical trials may fail to support the analytical and clinical validation of the companion diagnostic. We and our future collaborators may encounter difficulties in developing, obtaining regulatory approval for, manufacturing and commercializing companion diagnostics similar to those we face with respect to our therapeutic candidates and therapeutics themselves, including issues with achieving regulatory clearance or approval, production of sufficient quantities at commercial scale and with appropriate quality standards, and in gaining market acceptance. If we are unable to successfully develop companion diagnostics for these therapeutic product candidates, or experience delays in doing so, the development of these therapeutic product candidates may be adversely affected, these therapeutic product candidates may not obtain marketing approval, and we may not realize the full commercial potential of any of these therapeutics that have or may 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 contract may decide to discontinue selling or manufacturing the companion diagnostic test that we anticipate using in connection with development and commercialization of our product candidates or our relationship with such diagnostic company may otherwise terminate. We 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 product candidates or do so on commercially reasonable terms, which could adversely affect and/or delay the development or commercialization of our therapeutic candidates.

If approved, our investigational products regulated as biologics may face competition from biosimilars approved through an abbreviated regulatory pathway.

The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively the ACA, includes a subtitle called the Biologics Price Competition and Innovation Act of 2009, or BPCIA, which created an abbreviated approval pathway for biological products that are biosimilar to or interchangeable with an FDA-licensed reference biological product. Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date that the reference product was first licensed by the FDA. In addition, the approval of a biosimilar product may not be made effective by the FDA until 12 years from the date on which the reference product was first licensed. During this 12-year period of exclusivity, another company may still market a competing version of the reference product if the FDA approves a BLA for the competing product containing the sponsor’s own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity, and potency of the other company’s product. The law is complex and is still being interpreted and implemented by the FDA. As a result, its ultimate impact, implementation, and meaning are subject to uncertainty.

We believe that any of our product candidates approved as a biological product 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 our investigational medicines to be reference products for competing products, 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, once licensed, will be substituted for any one of our reference products in a way that is similar to traditional generic substitution for non-biological products 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 of our product candidates, our products may become subject to competition from such biosimilars, which would impair our ability to successfully commercialize and generate revenues from sales of such products.

Our product candidates, if approved, will be, subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our product candidates.

Our product candidates, if approved, will be, subject to ongoing regulatory requirements and review by the FDA and other applicable regulatory authorities 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 and 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 will be subject to continual review and inspections to assess compliance with cGMP and adherence to commitments made in any NDA, BLA or marketing authorization application, or MAA. 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. Furthermore, under the Drug Supply Chain Security Act, for certain commercial prescription drug products, manufacturers and other parties involved in the supply chain must also meet chain of distribution requirements and build electronic, interoperable systems for product tracking and tracing and for notifying the FDA of counterfeit, diverted, stolen, and intentionally adulterated products or other products that are otherwise unfit for distribution in the U.S. In addition, the distribution of prescription pharmaceutical products, including samples, is subject to the Prescription Drug Marketing Act, or PDMA, which regulates the distribution of drugs and drug samples at the federal level, and sets minimum standards for the registration and regulation of drug distributors by the states. Both the PDMA and state laws limit the distribution of prescription pharmaceutical product samples and impose requirements to ensure accountability in distribution. Prescription drug products must also meet applicable child-resistant packaging requirements under the U.S. Poison Prevention Packaging Act. If we are not able to comply with post-approval regulatory requirements, we could have the marketing approvals for any approved products withdrawn by regulatory authorities and our ability to market such products could be limited, which could adversely affect our ability to achieve or sustain profitability and we could be subject to substantial penalties. As a result, the cost of compliance with post-approval regulations may have a negative effect on our operating results and financial condition.

Any regulatory approvals that we may receive for our product candidates, are or will be subject to limitations on the approved indicated uses for which the product may be marketed and promoted or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase 4 clinical trials and surveillance to monitor the safety and efficacy of the product. We will be required to report certain adverse reactions and production problems, if any, to the FDA and comparable foreign regulatory authorities. Any new legislation addressing drug safety issues could result in delays in product development or commercialization, or increased costs to assure compliance. Additionally, under FDORA, sponsors of approved drugs and biologics must provide six months' notice to the FDA of any changes in marketing status, such as the withdrawal of a drug, and failure to do so could result in the FDA placing the product on a list of discontinued products, which would revoke the product's ability to be marketed.

The FDA and other agencies, including the Department of Justice, closely regulate and monitor the post-approval marketing, labeling, advertising and promotion of products to ensure that they are manufactured, marketed and distributed only for the approved indications and in accordance with the provisions of the approved label. We are required to comply with requirements concerning advertising and promotion for products that may be approved. Promotional communications with respect to prescription drugs are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product's approved label. As such, we may not promote those products for indications or uses for which they do not have approval.

The holder of an approved NDA, BLA or MAA must submit new or supplemental applications and obtain approval for certain changes to the approved product, product labeling, or manufacturing process. We could also be asked to conduct post-marketing clinical trials to verify the safety and efficacy of our products, if approved in general or in specific patient subsets. If original marketing approval was obtained via the accelerated approval pathway, we could be required to conduct a successful post-marketing clinical trial to confirm clinical benefit for those products.

If a regulatory agency discovers previously unknown problems with a product, such as AEs of unanticipated severity or frequency, or problems with the facility where the product is manufactured, or disagrees with the promotion, marketing or labeling of a product, such regulatory agency may impose restrictions on that product or us, including requiring withdrawal of the product from the market. If we fail to comply with applicable regulatory requirements, a regulatory agency or enforcement authority may, among other things:

- issue warning or untitled letters that would result in adverse publicity;
- impose civil or criminal penalties;
- suspend or withdraw regulatory approvals;
- suspend any of our ongoing clinical trials;
- refuse to approve pending applications or supplements to approved applications submitted by us;
- impose restrictions on our operations, including closing our CMOs' facilities;
- impose restrictions on the labeling of products;
- impose restrictions on product distribution or use, such as a REMS;
- seize or detain products; or
- require a product 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 products. If regulatory sanctions are applied or if regulatory 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 approval of our product candidates or suspend, withdraw or modify regulatory approval of our products.

The FDA and other regulatory agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses.

If any of our current product candidates are approved and we are found to have improperly promoted off-label uses of our products, we may become subject to significant liability. The FDA and other regulatory agencies strictly regulate the promotional claims that may be made about prescription products. In particular, while the FDA permits the dissemination of truthful and non-misleading information about an approved product, a sponsor may not promote a product for uses that are not approved by the FDA or such other regulatory agencies as reflected in the product's 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 our product candidates, if approved, we could become subject to significant liability, which would materially adversely affect our business and financial condition.

Notwithstanding regulations related to product promotion, the FDA and other regulatory authorities allow companies to engage in truthful, non-misleading, and non-promotional scientific exchange concerning their products. We intend to engage in medical education activities and communicate with healthcare providers in compliance with all applicable laws and regulatory guidance.

Risks Related to the Novel Nature of our Product Candidates

Certain of our product candidates, including our protein therapeutic and gene therapy product candidates, 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 product candidates, including our protein therapeutic and gene therapy product candidates, are complex, novel and have not been validated for commercial use. Several factors have caused and may cause future production interruptions, including restrictions on certain manufacturing operations and shortages in on-site personnel at our CMOs' manufacturing facilities as a result of governmental "stay at home" orders in response to the COVID-19 pandemic, 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.

Several of our small molecule product candidates are particularly complex and difficult to manufacture, in some cases due to the number of steps required, the process complexity and the toxicity of end or intermediate-stage products. Our protein therapeutic and gene therapy product candidates require processing steps that are more complex than those required for most small molecule drugs. Moreover, unlike small molecules, the physical and chemical properties of certain of our biologic product candidates generally cannot be fully characterized. As a result, assays of the finished product may not be sufficient to ensure that the product 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 product 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 product defects or manufacturing failures that result in lot failures, product recalls, product liability claims or insufficient inventory to conduct clinical trials or supply commercial markets. We 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 to submit samples of any lot of any approved product 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 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 product that could result in lot failures or product recalls. Lot failures or product recalls could cause us to delay product 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 also restrict our ability to meet potential future market demand for any products that may be approved.

Certain of our product candidates are based on a novel adeno-associated virus, or AAV, gene therapy technology with which there is limited clinical or regulatory experience to date, which makes it difficult to predict the time and cost of product candidate development and subsequently obtaining regulatory approval.

Certain of our product candidates are based on gene therapy technology and our future success depends on the successful development of this novel therapeutic approach. We cannot assure you that any development problems we or other gene therapy companies experience in the future related to gene therapy technology will not cause significant delays or unanticipated costs in the development of our product candidates, or that such development problems can be solved. In addition, the clinical study requirements of the FDA, the EMA and other regulatory agencies and the criteria these regulators use to determine the safety and efficacy of a product candidate vary substantially according to the type, complexity, novelty and intended use and market of the potential products. The regulatory approval process for novel product candidates such as ours can be more expensive and take longer than for other, better known or extensively studied therapeutic modalities. Further, as we are developing novel treatments for diseases in which there is limited clinical experience with new endpoints and methodologies, there is heightened risk that the FDA, the EMA or comparable foreign regulatory bodies may not consider the clinical trial endpoints to provide clinically meaningful results, and the resulting clinical data and results may be more difficult to analyze. To date, few gene therapy products have been approved by the FDA or comparable foreign regulatory authorities, which makes it difficult to determine how long it will take or how much it will cost to obtain regulatory approvals for our product candidates in the United States, the European Union or other jurisdictions. Further, approvals by one regulatory agency may not be indicative of what other regulatory agencies may require for approval.

Regulatory requirements governing the development of gene therapy products have changed frequently and may continue to change in the future. In 2016, the FDA established the Office of Tissues and Advanced Therapies, or OTAT, within its Center for Biologics Evaluation and Research, or CBER, to consolidate the review of gene therapy and related products, and to advise CBER on its review. In September 2022, the FDA announced retitling of OTAT to the Office of Therapeutic Products, or OTP, and elevation of OTP to a “Super Office” to meet its growing cell and gene therapy workload. In addition, under guidelines issued by the National Institutes of Health, or NIH, gene therapy clinical trials are also subject to review and oversight 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. Before a clinical trial can begin at any institution, that institution’s institutional review board, or IRB, and its IBC assesses the safety of the research and identifies any potential risk to public health or the environment. 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. Moreover, serious adverse events or developments in clinical trials of gene therapy product candidates conducted by others may cause the FDA or other regulatory bodies to initiate a clinical hold on our clinical trials or otherwise change the requirements for approval of any of our product candidates. Although the FDA decides whether individual cell and gene therapy protocols may proceed, the review process and determinations of other reviewing bodies can impede or delay the initiation of a clinical trial, even if the FDA has reviewed the trial and approved its initiation.

Similarly, the EMA governs the approval of gene therapies in the European Union and may issue new guidelines concerning the development and marketing authorization for gene therapy products and require that we comply with these new guidelines.

These regulatory review committees and advisory groups and the new guidelines they promulgate may lengthen the regulatory review process, require us to perform additional studies or trials, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of our product candidates or lead to significant post-approval limitations or restrictions. As we advance our product candidates, we will be required to consult with these regulatory and advisory groups and comply with applicable guidelines. If we fail to do so, we may be required to delay or discontinue development of such product candidates. These additional processes may result in a review and approval process that is longer than we otherwise would have expected. Delays as a result of an increased or lengthier regulatory approval process or further restrictions on the development of our product candidates can be costly and could negatively impact our ability to complete clinical trials and commercialize our current and future product candidates, if approved, in a timely manner, if at all.

Our product candidates based on gene therapy technology may cause undesirable and unforeseen side effects or be perceived by the public as unsafe, which could delay or prevent their advancement into clinical trials or regulatory approval, the imposition of a clinical hold, limit the commercial potential or result in significant negative consequences.

Public attitudes may be influenced by claims that gene therapy as a novel technology is unsafe, unethical, or immoral, and, consequently, our product candidates may not gain the acceptance of the public or the medical community. Adverse public attitudes may adversely impact our ability to enroll clinical trials. In addition, the FDA has imposed an increased number of clinical holds on gene therapy candidates in recent years. Moreover, our success will depend upon physicians prescribing, and their patients being willing to receive, treatments that involve the use of product candidates we may develop in lieu of, or in addition to, existing treatments with which they are already familiar and for which greater clinical data may be available. For example, there have been several significant adverse side effects in prior clinical trials of gene therapy product candidates, including reported cases of leukemia and death seen in other trials using other vectors. While new AAV vectors have been developed to reduce these side effects, gene therapy is still a relatively new approach to disease treatment and additional adverse side effects could develop. There also is the potential risk of delayed AEs following exposure to gene therapy products due to persistent biologic activity of the genetic material or other components of products used to carry the genetic material.

Possible adverse side effects that could occur with treatment with gene therapy products include an immunologic reaction early after administration which could be detrimental to the patient's health or substantially limit the effectiveness and durability of the treatment. For example, an increasingly anticipated side effect of AAV gene therapy is the development of a T-cell immunological response, most often seen affecting the liver. Any actual or perceived negative effects of our AAV gene therapy product candidates or those under development by third parties could impair our ability to continue the development of these product candidates and have an adverse effect on our prospects.

Risks Related to Our Reliance on Third Parties

We expect to rely on third parties to conduct 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 will delay our product development activities.

Our reliance on these third parties for research and development activities reduces control over these activities but does not relieve us of our responsibilities. For example, we remain responsible for ensuring that each of our respective clinical trials is conducted in accordance with the general investigational plan and protocols for the trial and applicable legal, regulatory, and scientific standards, and our reliance on third parties does not relieve us of our regulatory responsibilities. In addition, the FDA and comparable foreign regulatory authorities require compliance with GCPs for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible, reproducible and accurate and that the rights, integrity and confidentiality of trial participants are protected. Regulatory authorities enforce these GCPs through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of these third parties fail to comply with applicable GCP regulations, some or all of the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to perform additional nonclinical or clinical trials or to enroll additional patients before approving our marketing applications. We cannot be certain that, upon inspection, such regulatory authorities will determine that any of our clinical trials complies with the GCP regulations. For any violations of laws and regulations during the conduct of clinical trials, we could be subject to untitled and warning letters or enforcement action that may include civil penalties up to and including criminal prosecution. We also are required to register ongoing clinical trials and post the results of completed clinical trials on a government-sponsored database within certain timeframes. Failure to do so can result in fines, adverse publicity, and civil and criminal sanctions.

If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct clinical trials in accordance with regulatory requirements or our stated protocols, we will not be able to obtain, or may be delayed in obtaining, marketing approvals for any product candidates we may develop and will not be able to, or may be delayed in our efforts to, successfully commercialize our medicines. Our failure or the failure of these third parties to comply applicable regulatory requirements or our stated protocols could also subject us to enforcement action.

We also expect to rely on other third parties to store and distribute drug supplies for our clinical trials. Any performance failure on the part of our distributors could delay clinical development or marketing approval of any product candidates we may develop or commercialization of our medicines, producing additional losses and depriving us of potential product revenue.

We rely entirely on third parties for the manufacturing of our current product candidates or other product candidates that we may develop for preclinical studies and clinical trials. Our business could be harmed if those third parties fail to provide us with sufficient quantities of drug product, or fail to do so at acceptable quality levels or prices.

We 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 may conduct, and we lack the resources to manufacture our product candidates, if approved, on a commercial scale. We rely, and expect to continue to rely, on third-party manufacturers to produce our current product candidates or other product candidates that we may identify for clinical trials, as well as for commercial manufacture of any product candidates that may receive marketing approval. Although we generally do not begin a clinical trial unless we believe we have a sufficient supply of a product candidate to complete the trial, any significant delay or discontinuity in the supply of a product 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 approval of our product candidates, which could harm our business and results of operations. We also expect to rely primarily on third parties for the manufacturing of commercial supply of our product candidates, if approved.

We 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 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.

Furthermore, all of our CMOs are engaged with other companies to supply and/or manufacture materials or products for such companies, which exposes our manufacturers to regulatory risks for the production of such materials and products. The facilities used by our contract manufacturers to manufacture our product candidates are subject to review by the FDA pursuant to inspections that will be conducted after we submit an NDA or BLA to the FDA. We do not control the manufacturing process of, and are completely dependent on, our contract manufacturing partners for compliance with the regulatory requirements, known as cGMP, requirements for manufacture of drug and biologic products. 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 approval for our product 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 or a comparable foreign regulatory agency does not approve these facilities for the manufacture of our product candidates or if any agency withdraws its approval in the future, we may need to find alternative manufacturing facilities, which would negatively impact the ability to develop, obtain regulatory approval for or market, if approved, our product candidates.

On March 27, 2020, President Trump signed into law the CARES Act in response to the COVID-19 pandemic. Throughout the COVID-19 pandemic, there has been public concern over the availability and accessibility of critical medical products, and the CARES Act enhances FDA's existing authority with respect to drug shortage measures. Under the CARES Act, we must have in place a risk management plan that identifies and evaluates the risks to the supply of approved drugs for certain serious diseases or conditions for each establishment where the drug or active pharmaceutical ingredient is manufactured. The risk management plan will be subject to FDA review during an inspection. If we experience shortages in the supply of our product candidates that receive marketing approval, our results could be materially impacted.

Our product candidates may compete with other product candidates and marketed drugs for access to manufacturing facilities. For example, since the beginning of the COVID-19 pandemic, several vaccines for COVID-19 have received Emergency Use Authorization by the FDA and a number of those later received marketing approval. Additional vaccines may be authorized or approved in the future. 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 products needed for our clinical trials, which could lead to delays in these trials or issues with commercial supply. Any performance failure on the part of our existing or future manufacturers could delay clinical development, marketing approval or commercialization. Our current and anticipated future dependence upon others for the manufacturing of our product candidates may adversely affect our future profit margins and our ability to commercialize any product candidates that receive marketing approval on a timely and competitive basis.

The drug substance and drug product for certain of our product candidates are currently acquired from single-source suppliers. The loss of these suppliers, or their failure to supply us with the drug substance or drug product, could materially and adversely affect our business.

The drug substance and drug product for certain of our product candidates are manufactured by single-source suppliers or CMOs under development and manufacturing contracts and services and quality agreements and purchase orders. We do not currently have any other suppliers for the drug substance or drug product of these product candidates and, although we believe that there are alternate sources of supply that could satisfy our clinical and commercial requirements, we cannot assure you that identifying alternate sources and establishing relationships with such sources would not result in significant delay in the development of our product candidates.

Our dependence on single-source suppliers exposes us to certain risks, including the following:

- our suppliers may cease or reduce production or deliveries, raise prices or renegotiate terms;
- delays caused by supply issues may harm our reputation; and

- our ability to progress our business could be materially and adversely impacted if our single-source suppliers upon which we rely were to experience a significant business challenges, disruption or failures due to issues such as financial difficulties or bankruptcy, issues relating regulatory or quality compliance issues, or other legal or reputational issues.

Additionally, we may not be able to enter into supply arrangements with alternative suppliers on commercially reasonable terms, or at all. A delay in the development of our product candidates or having to enter into a new agreement with a different third party on less favorable terms than we have with our current suppliers could have a material adverse impact upon on our business.

If the contract manufacturing facilities on which we rely do not continue to meet regulatory requirements or are unable to meet our supply demands, our business will be harmed.

All entities involved in the preparation of product candidates for clinical trials or commercial sale, including our existing CMOs for all of our product candidates, are subject to extensive regulation. Components of a finished therapeutic product 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 products and products approved for sale. Poor control of production processes can lead to the introduction of contaminants or to inadvertent changes in the properties or stability of our product candidates. Our failure, or the failure of third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, suspension of production, seizures or recalls of product candidates or marketed drugs, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect clinical or commercial supplies of our product candidates.

We or our CMOs must supply all necessary documentation in support of an NDA, BLA 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 product 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 our product candidates or any of our other potential products. In addition, the regulatory authorities may, at any time, audit or inspect a manufacturing facility involved with the preparation of our product candidates or our other potential products 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 applicable product candidates 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 approval of a product 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 product 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 trial 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 through an NDA, BLA supplement or MAA variation, or equivalent foreign regulatory filing, which could result in further delay. The regulatory agencies may also require additional studies if a new manufacturer is relied upon for commercial production. In some cases, the technical skills required to manufacture our product candidates may be unique or proprietary to the original CMO and we may have difficulty, or there may be contractual restrictions prohibiting us from, transferring such skills to a back-up or alternate supplier, or we may be unable to transfer such skills at all. In addition, if we are required to change CMOs for any reason, we will be required to verify that the new CMO 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 will produce our product or product candidate according to the specifications previously submitted to or approved by the FDA or another regulatory authority. The delays associated with the verification of a new CMO could negatively affect our ability to develop product candidates or once approved, to commercialize those product candidates in a timely manner or within budget. In addition, changes in manufacturers often involve changes in manufacturing procedures and processes, which could require that we conduct bridging studies between our prior clinical supply used in our clinical trials and that of any new manufacturer. We may be unsuccessful in demonstrating the comparability of clinical supplies, which could require the conduct of additional clinical trials. Accordingly, 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 to incur higher costs and could cause the delay or termination of clinical trials, regulatory submissions, required approvals, or commercialization of our product candidates. Furthermore, if our suppliers fail to meet contractual requirements and we are unable to secure one or more replacement suppliers capable of production at a substantially equivalent cost, our clinical trials may be delayed or we could lose potential revenue.

Collaborative relationships with third parties could cause us to expend significant resources and incur substantial business risk with no assurance of financial return.

We anticipate relying upon strategic collaborations for marketing and commercializing our existing product candidates. For example, Eidos is party to a license agreement with Alexion Pharma International Operations Unlimited Company, or Alexion, pursuant to which we depend on Alexion for the clinical development and commercialization of acoramidis in Japan, and QED has previously entered into a license and collaboration agreement with Helsinn Healthcare S.A. and Helsinn Therapeutics (U.S.), Inc., to which we refer collectively as Helsinn, pursuant to which QED granted to Helsinn exclusive licenses to develop, manufacture and commercialize QED's product candidate, infigratinib, in oncology and all other indications except achondroplasia or any other skeletal dysplasias, worldwide (except for the People's Republic of China, Hong Kong and Macau for which regions QED has entered into a partnership with LianBio). We subsequently received a notice of termination of the collaboration from Helsinn, citing commercial considerations. In December 2022, we signed a mutual termination agreement. In addition, we may rely even more on strategic collaborations for R&D of other product candidates, and we may sell or license other product offerings through strategic partnerships with pharmaceutical and biotechnology companies.

If we enter into R&D collaborations during the early phases of product 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 product 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 products 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 collaborations, these relationships may never result in the successful development or commercialization of product candidates or the generation of sales revenue. To the extent that we enter into collaborative arrangements, the related product revenues are likely to be lower than if we directly marketed and sold such products. Such collaborators may also consider alternative product 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 product 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.

If we are unable to establish or maintain such strategic collaborations on terms favorable to us in the future, our R&D efforts and potential to generate revenue may be limited.

We are parties 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.

The success of our 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 our product candidates 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 products or their internal development of competitive products, 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 development program, stop a clinical trial, abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our products or product candidates;
- a collaborator with marketing, manufacturing and distribution rights to one or more products 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 product 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 products or product candidates;
- collaborators may own or co-own intellectual property covering products 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 our product candidates, due to capital costs required to develop or commercialize the product candidate or manufacturing constraints. We may not be successful in our efforts to establish such collaborations for our product candidates because our research and development pipeline may be insufficient, our product candidates may be deemed to be at too early of a stage of development for collaborative effort or third parties may not view our product candidates 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 product candidate is delayed, the safety of a product candidate is questioned or sales of an approved product candidate are unsatisfactory. For example, on August 23, 2022, we received written notice from Helsinn Group, or Helsinn, of its intent to terminate the Amended and Restated License and Collaboration Agreement ("Amended QED-Helsinn License and Collaboration Agreement") for convenience, pursuant to its terms, citing commercial considerations, and in December 2022 we entered into a mutual termination agreement with Helsinn.

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 our product candidates, 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 our product candidates, could delay the development and commercialization of our product candidates 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.

Risks Related to Our Intellectual Property

If we are unable to obtain and maintain sufficient intellectual property protection for our product candidates, including acoramidis, low-dose infigratinib, BBP-418, BBP-631, encaleret and any KRAS inhibitor candidates, or if the scope of the intellectual property protection obtained is not sufficiently broad, our competitors could develop and commercialize products or product candidates similar or identical to ours, and our ability to successfully commercialize our product candidates 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 product candidates and technology. We seek to protect our proprietary position by filing patent applications in the United States and abroad related to our product candidates.

Obtaining and enforcing pharmaceutical and biopharmaceutical patents is costly, time consuming and complex, and we may not be able to file and prosecute all necessary or desirable patent applications, or maintain, enforce and license any patents that may issue from such patent applications, at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. 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. 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. Further, we may not be aware of all third-party intellectual property rights potentially relating to our product candidates. 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. 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, product 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 ability to develop and market our product candidates. We do not always conduct independent reviews of pending patent applications of and patents issued to third parties. 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 product candidates, in whole or in part, or which effectively prevent others from commercializing competitive products. 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 product candidates in a non-infringing manner.

Our ability to enforce patent rights also 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 products and services. Moreover, it may be difficult or impossible to obtain evidence of infringement in a competitor's or potential competitor's product 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 initiate lawsuits to protect or enforce our patents, or litigate against third-party claims, such proceedings would be expensive and would divert the attention of our management and technical personnel. Such proceedings could also provoke third parties to assert claims against us, including that some or all of the claims in one or more of our patents are invalid or otherwise unenforceable.

Moreover, we may be subject to a third-party preissuance submission of prior art to the United States Patent and Trademark Office, or the USPTO, or become involved in opposition, derivation, reexamination, *inter partes* review, post-grant review or interference proceedings challenging our patent rights or the patent rights of others. 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 product 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 product candidates.

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 product candidates to ours, or limit the duration of the patent protection of our product candidates. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such product candidates might expire before or shortly after such product candidates are commercialized. As a result, our patent portfolio may not provide us with sufficient rights to exclude others from commercializing drugs similar or identical to ours.

Furthermore, our intellectual property rights may be subject to a reservation of rights by one or more third parties. For example, the research resulting in certain of our patent rights and technology was funded in part by the U.S. government. As a result, the government has certain rights, including march-in rights, to such patent rights and technology. 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 products 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.

Our rights to develop and commercialize our product candidates are subject in part to the terms and conditions of licenses granted to us by others, and the patent protection, prosecution and enforcement for some of our product candidates may be dependent on our licensors.

We currently are reliant upon licenses of certain intellectual property rights and proprietary technology from third parties that are important or necessary to the development of our proprietary technology, including technology related to product candidates. These licenses, and other licenses we may enter into in the future, may not provide adequate rights to use such intellectual property rights and proprietary technology in all relevant fields of use or in all territories in which we may wish to develop or commercialize technology, and product candidates in the future. Licenses to additional third-party proprietary technology or intellectual property rights that may be required for our development programs may not be available in the future or may not be available on commercially reasonable terms. In that event, we may be required to expend significant time and resources to redesign our proprietary technology or product candidates or to develop or license replacement technology, which may not be feasible on a technical or commercial basis. If we are unable to do so, we may not be able to develop and commercialize technology, and product 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 may not have the right to control the preparation, filing, prosecution and enforcement of patent applications, or to maintain the patents, covering technology that we license from third parties. In addition, some of our 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 product candidates. We 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 product candidates may be adversely affected and we may be unable to prevent competitors from making, using and selling competing products.

In addition, our 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 products, if any, the amounts may be significant. The amount of our future royalty obligations will depend on the technology and intellectual property we use in our product candidates that we successfully develop and commercialize. Therefore, even though we have previously developed and commercialized two approved products, we did not generate significant revenues from sales of those products, and may be unable to achieve or maintain profitability with any future product candidates that we may commercialize. In addition, we 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 existing licenses. Any of these events could have a material adverse effect on our competitive position, business, financial condition, results of operations, and prospects

If we 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 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 operate our business, 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 compliance with the terms of these agreements. For example, we are a party to an exclusive license agreement with the Board of Trustees of the Leland Stanford Junior University, or Stanford, and may need to obtain additional licenses from others to advance our research and development activities to allow the commercialization of acoramidis or any other product candidates we may identify and pursue. Our license agreement with Stanford imposes, and we expect that future license agreements will impose, various development, diligence, commercialization, and other obligations on us. In particular, under our license agreement with Stanford, we are required to use commercially reasonable efforts to engage in various development and commercialization activities with respect to licensed products, and must satisfy specified milestone and royalty payment obligations. We are also a party to a license agreement with Novartis International Pharmaceutical Ltd. for infigratinib under which we are required to use commercially reasonable efforts to develop infigratinib, and to obtain regulatory approval for and commercialize at least one therapeutic product incorporating infigratinib in the United States and the European Union. We obtained regulatory approval for TRUSELTIQ in the United States in May 2021.

In spite of our efforts, our 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 ability to develop and commercialize products and technology covered by these license agreements. For example, if our license agreement with Stanford is terminated, competitors or other third parties would have the freedom to seek regulatory approval of, and to market, products identical to acoramidis and we may be required to cease our development and commercialization of acoramidis. Any of the foregoing could have a material adverse effect on our competitive position, business, financial condition, results of operations and prospects.

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 product 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 collaborative development relationships;
- our 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 licensors and us and our partners; and
- the priority of invention of patented technology.

In addition, certain provisions in our 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 business, financial condition, results of operations and prospects. Moreover, if disputes over intellectual property that we 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 product candidates, which could have a material adverse effect on our competitive position, business, financial condition, 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 in the courts, and interferences, oppositions and *inter partes* reexamination proceedings 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. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that acoramidis, low-dose infigratinib, BBP-418, BBP-631, encaleret, any KRAS inhibitor candidates or other product candidates that we may identify may be subject to claims of infringement of the patent rights of third parties.

Other third parties may assert that we are employing their proprietary technology without authorization. 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 product candidates. 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 product candidates may infringe. In addition, third parties may obtain patents in the future and claim that use of our 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 product candidates, any molecules formed during the manufacturing process or any final product itself, the holders of any such patents may be able to block our ability to commercialize such product or product candidate unless we obtained a license under the applicable patents, or until such patents expire.

Similarly, if any third-party patents were held by a court of competent jurisdiction to cover aspects of our formulations, processes for manufacture or methods of use, including combination therapy, the holders of any such patents may be able to block our ability to develop and commercialize the applicable product or product 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 rights.

Parties making claims against us may obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize our product candidates. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys’ fees for willful infringement, pay royalties, redesign our infringing products 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 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 ability to raise additional funds or otherwise have a material adverse effect on our business, results of operations, financial condition and prospects.

Patent terms may be inadequate to protect our competitive position on product 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 product candidates are obtained, once the patent life has expired, we may be open to competition from competitive products, including generics or biosimilars. Given the amount of time required for the development, testing and regulatory review of products or new product candidates, patents protecting such products or candidates might expire before or shortly after such products or candidates are commercialized. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

If we are not able to obtain, or in applicable cases maintain, 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 our product candidates, our business may be materially harmed.

Depending upon the timing, duration and specifics of FDA marketing approval of our product candidates, one of the U.S. patents covering each of such products or product 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 FDA approved product 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 product approval and only those claims covering such approved drug product, 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 our product candidates. Nevertheless, we 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 are unable to obtain patent term extension, or the term of any such extension is less than we request, the period during which we will have the right to exclusively market any products that may be approved, may be shortened and our competitors may obtain approval of competing products following our patent expiration sooner, and our revenue could be reduced, possibly materially.

It is possible that we will not obtain patent term extension under the Hatch-Waxman Act for a U.S. patent covering a product candidate even where that patent is eligible for patent term extension, or if we obtain such an extension, it may be for a shorter period than we had sought. Further, for certain of our licensed patents, we do not have the right to control prosecution, including filing with the USPTO, an application for patent term extension under the Hatch-Waxman Act. Thus, if one of our licensed patents is eligible for patent term extension under the Hatch-Waxman Act, we may not be able to control whether an application to obtain a patent term extension is filed, or an extension 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 may be unable to obtain patents covering our product candidates that contain one or more claims that satisfy the requirements for listing in the Orange Book. Even if we 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 one of our current product candidates is approved and a patent covering that product 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 product.

Depending upon the timing and specifics of marketing approval of our products, the FDA and other applicable regulatory authorities may grant certain non-patent exclusivities. Although we intend to seek new chemical entity exclusivity, and potentially other exclusivities, for product candidates we are developing, we may not be successful in doing so. Moreover, these non-patent exclusivities, if granted, are limited and other companies may be able to submit marketing applications and receive approval earlier than we anticipate.

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 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 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 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 confidential proprietary information 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.

Unauthorized parties may also attempt to copy or reverse engineer certain aspects of our product candidates that we consider proprietary. We 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 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 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 this information may be greatly reduced and our competitive position, business, financial condition, results of operations, and prospects would be harmed.

If our 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 registered or unregistered trademarks or trade names, may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. We 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 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 may license our trademarks and trade names to third parties, such as distributors. Though these license agreements may provide guidelines for how our 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 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 become involved in lawsuits to protect or enforce our patents or other intellectual property, which could be expensive, time consuming and unsuccessful.

Competitors may infringe our patents or other intellectual property. If we were to initiate legal proceedings against a third party to enforce a patent covering one or more of our product candidates, the defendant could counterclaim that the patent covering our product 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 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 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, enter into development partnerships that would help us bring product 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 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 have a material adverse effect on the price of our common stock.

We may be subject to claims challenging the inventorship of our patents and other intellectual property.

Our 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 enter into 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 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 or our licensors may have inventorship disputes arise from conflicting obligations of employees, consultants or others who are involved in developing our product candidates. Litigation may be necessary to defend against these and other claims challenging inventorship or our or our licensors' ownership of our owned or in-licensed patents, trade secrets or other intellectual property. If we 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 product 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.

Issued patents covering our product candidates could be found invalid or unenforceable if challenged in court.

If we or one of our licensing partners initiated legal proceedings against a third party to enforce a patent covering one or more of our product candidates, the defendant could counterclaim that the patent covering the relevant product 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 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 patents in such a way that they no longer cover our products or product 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 product candidates. Such a loss of patent protection would have a material adverse impact on our business.

We 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 industry, we employ individuals who were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we 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 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 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 are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

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 have systems in place to remind us to pay these fees, and we employ an outside firm and rely on outside counsel to pay these fees due to non-U.S. patent agencies. However, we cannot guarantee that our licensors have similar systems and procedures in place to pay such fees. 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.

We may not be able to protect our intellectual property rights throughout the world.

Filing, prosecuting and defending patents on our product 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 intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and may also export infringing products to territories where we have patent protection, but enforcement is not as strong as that in the United States. These products may compete with our products, 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 products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our 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 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. We may not prevail in any lawsuits that we 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.

Changes in U.S. patent law could diminish the value of patents in general, thereby impairing our ability to protect our products.

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 to be cognizant of the time from invention to filing of a patent application. 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 or our licensors were the first to either (i) file any patent application related to our product candidates or (ii) invent any of the inventions claimed in our 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 United States 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 federal 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 federal district court action. Therefore, the America Invents Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our owned or in-licensed patent applications and the enforcement or defense of our 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 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 rights in the future.

Risks Related to Commercialization

Our product candidates, if approved, may fail to achieve the degree of market acceptance by physicians, patients, healthcare payors, and others in the medical community necessary for commercial success.

The commercial success of our product candidates, if approved, will depend upon their degree of market acceptance by physicians, patients, third-party payors, and others in the medical community. Our product candidates, if approved, may nonetheless fail to gain sufficient market acceptance by physicians, patients, healthcare payors, and others in the medical community. The degree of market acceptance of our product candidates we may develop, if approved for commercial sale, will depend on a number of factors, including:

- the efficacy and safety of such product candidates as demonstrated in pivotal clinical trials and published in peer-reviewed journals;
- the potential and perceived advantages compared to alternative treatments, including any similar generic treatments;
- the ability to offer these products for sale at competitive prices;
- the ability to offer appropriate patient access programs, such as co-pay assistance;
- convenience and ease of dosing and administration compared to alternative treatments;
- the clinical indications for which the product candidate is approved by the FDA or comparable regulatory authorities;
- product labeling or product insert requirements of the FDA or other comparable foreign regulatory authorities, including any limitations, contraindications or warnings contained in a product's approved labeling;
- restrictions on how the product is distributed;
- the timing of market introduction of competitive products;
- publicity concerning these products or competing products and treatments;
- the strength of marketing and distribution support;
- favorable third-party coverage and sufficient reimbursement or other assistance for patients who are uninsured or underinsured; and
- the prevalence and severity of any side effects or AEs.

Sales of medical products 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 products are safe, therapeutically effective and cost effective. In addition, the inclusion or exclusion of products 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 products are safe, therapeutically effective and cost effective as compared with competing treatments. If any product candidates we develop do not achieve an adequate level of acceptance, we may not generate significant product revenue, and we may not become profitable.

If we are unable to establish sales and marketing capabilities or enter into agreements with third parties to sell and market any product candidates we may develop, we may not be successful in commercializing those product candidates if and when they are approved.

To achieve commercial success for any approved product for which we retain sales and marketing responsibilities, we must continue to develop a sales and marketing organization or outsource these functions to third parties. In the future, we may choose to grow our focused sales, marketing, and commercial support infrastructure to market and sell our product candidates, 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 product candidates, indications or geographic territories, including territories outside the United States, as we did with Helsinn in the case of TRUSELTIQ once it was approved, although there is no guarantee we will be able to enter into similar arrangements in the future 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 product launch. If the commercial launch of a product 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 product 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 products;
- the inability of reimbursement professionals to negotiate arrangements for formulary access, reimbursement, and other acceptance by payors;
- the inability to price products at a sufficient price point to ensure an adequate and attractive level of profitability;
- manufacturing disruptions that delay or prevent the launch of any approved products;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product 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 product revenue or the profitability of product revenue may be lower than if we were to market and sell any products we may develop internally. In addition, we may not be successful in entering into arrangements with third parties to commercialize, if approved, our product candidates 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 products 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 products, including those restricting off-label promotion. If we do not continue to build on our commercialization capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates, if approved.

The insurance coverage and reimbursement status of newly-approved products is uncertain. Our product candidates 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 adequate coverage and reimbursement for new or current products could limit our ability to market those products and decrease our ability to generate revenue.

The regulations that govern marketing approvals, pricing, coverage, and reimbursement for new drugs vary widely from country to country. In the United States, recently enacted 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 drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay our commercial launch of the product, possibly for lengthy time periods, and negatively impact the revenue we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates even if those product candidates may obtain marketing approval. See the section entitled, "*Business — Government Regulation — Coverage and Reimbursement*."

Our ability to successfully commercialize our product candidates also will depend in part on the extent to which coverage and adequate reimbursement for these products 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 products. Sales of these product candidates or other product candidates, if approved, that we may identify will depend substantially, both domestically and abroad, on the extent to which the costs of our product candidates 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 product 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.

Additionally, we may develop companion diagnostic tests for use with our product candidates. We, 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 product candidates, once approved. Even if we 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 product 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 product or product candidate or companion diagnostic for which we receive approval. Our inability to promptly obtain coverage and adequate reimbursement from both third-party payors for the companion diagnostic tests that we develop and for which we obtain regulatory approval could have a material and adverse effect on our business, financial condition, results of operations and prospects.

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 products. Arrangements with third-party payors and customers can expose pharmaceutical manufacturers to broadly applicable fraud and abuse and other healthcare laws and regulations, which may constrain the business or financial arrangements and relationships through which such companies sell, market and distribute pharmaceutical products. 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. See the section entitled, "*Business — Government Regulation — Other Regulatory Matters*."

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, the 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 our product candidates outside the United States will also likely subject us to foreign equivalents of the healthcare laws mentioned above, among other foreign laws.

Third party patient assistance programs that receive financial support from companies have become the subject of enhanced government and regulatory scrutiny. Government enforcement agencies have shown increased interest in pharmaceutical companies' product and patient assistance programs, including reimbursement support services, and a number of investigations into these programs have resulted in significant civil and criminal settlements. The U.S. government has established guidelines that suggest that it is lawful for pharmaceutical manufacturers to make donations to charitable organizations who provide co-pay assistance to Medicare patients, provided that such organizations, among other things, are bona fide charities, are entirely independent of and not controlled by the manufacturer, provide aid to applicants on a first-come basis according to consistent financial criteria and do not link aid to use of a donor's product. However, donations to patient assistance programs have received some negative publicity and have been the subject of multiple government enforcement actions, related to allegations regarding their use to promote branded pharmaceutical products over other less costly alternatives. Specifically, in recent years, there have been multiple settlements resulting out of government claims challenging the legality of their patient assistance programs under a variety of federal and state laws. It is possible that we may make grants to independent charitable foundations that help financially needy patients with their premium, co-pay, and co-insurance obligations. If we choose to do so, and if we or our vendors or donation recipients are deemed to fail to comply with relevant laws, regulations or evolving government guidance in the operation of these programs, we could be subject to damages, fines, penalties, or other criminal, civil, or administrative sanctions or enforcement actions. We cannot ensure that our compliance controls, policies, and procedures will be sufficient to protect against acts of our employees, business partners, or vendors that may violate the laws or regulations of the jurisdictions in which we operate. Regardless of whether we have complied with the law, a government investigation could impact our business practices, harm our reputation, divert the attention of management, increase our expenses, and reduce the availability of foundation support for our patients who need assistance. Further, it is possible that changes in insurer policies regarding co-pay coupons and/or the introduction and enactment of new legislation or regulatory action could restrict or otherwise negatively affect these patient support programs, which could result in fewer patients using affected products, and therefore could have a material adverse effect on our sales, business, and financial condition. Although a number of these and other proposed measures may require authorization through additional legislation to become effective, and the current U.S. presidential administration may reverse or otherwise change these measures, both the current U.S. presidential administration and Congress have indicated that they will continue to seek new legislative measures to control drug costs. We cannot predict how the implementation of and any further changes to this rule will affect our business.

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 the Health Information Technology for Economic and Clinical Health Act of 2009, or 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.

California recently enacted the California Consumer Privacy Act, or CCPA, which creates new individual privacy rights for California consumers (as defined in the law) and places increased privacy and security obligations on entities handling personal data of consumers or households. Further, a new privacy law, the California Privacy Rights Act, or CPRA, was passed by California voters on November 3, 2020. The CPRA will create additional obligations relating to personal information effective January 1, 2023 (with certain provisions having retroactive effect to January 1, 2022). While the legislation and proposed regulations include the CCPA and CPRA contain an exception for activities that are subject to HIPAA, we cannot yet determine the impact the CCPA, CPRA or other such future laws, regulations and standards may have on our business. The uncertainty surrounding the implementation of the CCPA, CPRA and other similar laws, regulations and standards that may be adopted in other jurisdictions exemplifies the vulnerability of our business to the evolving regulatory environment related to personal data and protected health information. Compliance with U.S. and international data protection laws and regulations 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.

Additionally, some observers have noted that the CCPA and CPRA could mark the beginning of a trend toward more stringent privacy legislation in the U.S., which could increase our potential liability and adversely affect our business. Already, in the United States, we have witnessed significant developments at the state level. For example, on March 2, 2021, Virginia enacted the CDPA and, on July 8, 2021, Colorado's governor signed the CPA, into law. The CDPA and the CPA both became effective January 1, 2023. While the CDPA and CPA incorporate many similar concepts of the CCPA and CPRA, there are also several key differences in the scope, application, and enforcement of the law that will change the operational practices of regulated businesses. The new laws will, among other things, impact how regulated businesses collect and process personal sensitive data, conduct data protection assessments, transfer personal data to affiliates, and respond to consumer rights requests

A number of other states have proposed new privacy laws, some of which are similar to the above discussed recently passed laws. Such proposed legislation, if enacted, may add additional complexity, variation in requirements, restrictions and potential legal risk, require additional investment of resources in compliance programs, impact strategies and the availability of previously useful data and could result in increased compliance costs and/or changes in business practices and policies. The existence of comprehensive privacy laws in different states in the country would make our compliance obligations more complex and costly and may increase the likelihood that we may be subject to enforcement actions or otherwise incur liability for noncompliance.

The uncertainty surrounding the implementation of recent and emerging state privacy laws, regulations and standards that may be adopted in other jurisdictions exemplifies the vulnerability of our business to the evolving regulatory environment related to personal data and protected health information. Compliance with U.S. and international data protection laws and regulations 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.

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 additional clinical trials or continue to enroll subjects in our ongoing or future clinical trials in the European Union or in the UK, 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 UK GDPR. The GDPR 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 UK 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 UK GDPR, and the related national data protection laws of the European Union Member States may result in fines and other administrative penalties. The UK 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.

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 our product candidates or any future product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any product for which we obtain marketing approval. Changes in regulations, statutes or the interpretation of existing regulations could impact our business in the future by requiring, for example: (i) changes to our manufacturing arrangements; (ii) additions or modifications to product labeling; (iii) the recall or discontinuation of any products; or (iv) additional record-keeping requirements. If any such changes were to be imposed, they could adversely affect the operation of our business. See the section entitled, "*Business — Government Regulation — Current and Future Legislation*."

In addition, the Creating and Restoring Equal Access to Equivalent Samples Act, or CREATES Act, was enacted in 2019 requiring sponsors of approved NDAs and BLAs to provide sufficient quantities of product samples on commercially reasonable, market-based terms to entities developing generic drugs and biosimilar biological products. The law establishes a private right of action allowing developers to sue application holders that refuse to sell them product samples needed to support their applications. If we are required to provide product samples or allocate additional resources to responding to such requests or any legal challenges under this law, our business could be adversely impacted.

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 product candidates, if approved. Such reforms could have an adverse effect on anticipated revenue from product 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 product 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 our product candidates, if approved;
- our ability to receive or set a price that we believe is fair for our future products;
- 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.

We expect that the ACA, as well as other healthcare reform measures that may be adopted in the future, 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 product. 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 our product candidates, if approved.

Recent federal legislation and actions by state and local governments may permit reimportation of drugs from foreign countries into the United States, including foreign countries where the drugs are sold at lower prices than in the United States, which could materially adversely affect our operating results.

We may face competition in the United States for our product candidates if approved, from therapies sourced from foreign countries that have placed price controls on pharmaceutical products. In the United States, the Medicare Modernization Act contains provisions that may change U.S. importation laws and expand pharmacists' and wholesalers' ability to import cheaper versions of an approved drug and competing products from Canada, where there are government price controls. These changes to U.S. importation laws will not take effect unless and until the Secretary of the HHS certifies that the changes will pose no additional risk to the public's health and safety and will result in a significant reduction in the cost of products to consumers. Further, the MMA provides that these changes to U.S. importation laws will not take effect unless and until the Secretary of HHS certifies that the changes will pose no additional risk to the public's health and safety and will result in a significant reduction in the cost of products to consumers. On September 23, 2020, the Secretary of HHS made such certification to Congress, and on October 1, 2020, the FDA published a final rule that allows for the importation of certain prescription drugs from Canada. Under the final rule, States and Indian Tribes, and in certain future circumstances pharmacists and wholesalers, may submit importation program proposals to the FDA for review and authorization. Since the issuance of the final rule, on November 23, 2020, several industry groups filed federal lawsuits in the U.S. District Court for the District of Columbia, requesting injunctive relief to prevent implementation of the rule. Further, authorities in Canada have passed rules designed to safeguard the Canadian drug supply from shortages. On September 25, 2020, CMS stated drugs imported by States under this rule will not be eligible for federal rebates under Section 1927 of the Social Security Act and manufacturers would not report these drugs for "best price" or Average Manufacturer Price purposes. Since these drugs are not considered covered outpatient drugs, CMS further stated it will not publish a National Average Drug Acquisition Cost for these drugs. Separately, the FDA also issued a final guidance document outlining a pathway for manufacturers to obtain an additional National Drug Code, or NDC, for an FDA-approved drug that was originally intended to be marketed in a foreign country and that was authorized for sale in that foreign country. If implemented, importation of drugs from Canada may materially and adversely affect the price we receive for any of our product candidates. The regulatory and market implications of the final rule and guidance are unknown at this time. Proponents of drug reimportation may attempt to pass legislation that would directly allow reimportation under certain circumstances. Legislation or regulations allowing the reimportation of drugs, if enacted, could decrease the price we receive for any products that we may develop and adversely affect our future revenues and prospects for profitability. We will continue to monitor developments and their potential effect on our business.

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 product candidates we may develop and ultimately harm our financial condition.

The development and commercialization of new drug products is highly competitive. We may face competition with respect to any product 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 large pharmaceutical and biotechnology companies that are currently pursuing the development and commercialization of products for the treatment of the indications that our core value drivers are pursuing, including, but not limited to: tafamidis, a TTR tetramer stabilizer (presently marketed by Pfizer Inc. as Vyndamax and Vyndaqel), a competitor to acoramidis; vosoritide, a CNP analog (presently marketed by BioMarin Pharmaceutical Inc. as Voxzogo), a potential competitor to low-dose infigratinib as a treatment for achondroplasia; crinecerfont, a CRF1 receptor antagonist, a competitor to BBP-631; Natpara, a parathyroid hormone, a competitor to encaleret. If any of these or other competitors, including competitors for our other product candidates, receive FDA approval before we do, our product candidates 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 products 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 significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals, and marketing approved products than we do.

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 products that are safer, more effective, have fewer or less severe side effects, are more convenient, or are less expensive than any products that we may develop. Furthermore, currently approved products could be discovered to have application for treatment of our targeted disease indications or similar indications, which could give such products significant regulatory and market timing advantages over our product candidates. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours and may obtain orphan product 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, products or technologies developed by our competitors may render our product candidates uneconomical or obsolete and we may not be successful in marketing those product candidates, once approved, 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' products and our competitors may allege that our products infringe, misappropriate or otherwise violate their intellectual property. The availability of our competitors' products could limit the demand, and the price we are able to charge, for any products that we may develop and commercialize. See "Risks Related to Our Intellectual Property."

If the market opportunities for our product candidates are smaller than we believe they are, our revenue may be adversely affected, and our business may suffer. Our ability to successfully identify patients and acquire a significant market share will be necessary for us to achieve profitability and growth.

We focus research and product development on treatments for Mendelian diseases and genetically driven cancers, many of which are rare or orphan indications. Our projections of both the number of individuals who are affected by our target disease indications and have the potential to benefit from treatment with our product candidates, are based on our beliefs and estimates. These estimates have been derived from a variety of sources, including the scientific literature, and may prove to be incorrect. Further, new studies may change the estimated incidence or prevalence of these diseases. The number of patients may turn out to be lower than expected. The effort to identify patients with diseases we seek to treat is in early stages, and we cannot accurately predict the number of patients for whom treatment might be possible. Additionally, the potentially addressable patient population for our product candidates may be limited or may not be amenable to treatment with our products or product candidates, and new patients may become increasingly difficult to identify or gain access to, which would adversely affect our results of operations and our business. Further, even if we obtain significant market share for our product candidates under development in our key value driver programs, because the potential target populations are small, we may never achieve profitability despite obtaining such significant market share. In addition, market share could be limited by the availability of other treatments including Vyndamax (tafamidis) and Vyndaqel (tafamidis meglumine), for which Pfizer Inc. has been approved for the treatment of ATTR-CM the United States and Japan (Vyndaqel only). As a result, even if approved, acoramidis will not be the first treatment on the market for ATTR-CM, and its market share and potential to generate revenues may be limited.

Risks Related to Our Business and Industry

Our corporate restructuring initiative and the associated workforce reduction announced in January 2022 may not result in the full anticipated savings and may disrupt operations.

In January 2022, we committed to a restructuring initiative designed to drive operational changes in our business processes, efficiencies, and cost savings to advance our corporate strategy and development programs. The restructuring initiative included, among other components, consolidation and rationalization of our facilities, reprioritization of development programs and the reduction in our workforce. We may not fully realize the anticipated benefits, savings and improvements in our cost structure from our restructuring efforts due to unforeseen difficulties, delays or unexpected costs and the expenses of restructuring may be greater than anticipated. If we are unable to realize anticipated cost savings from the restructuring, our operating results and financial condition may be adversely affected. Furthermore, our reprioritization of development programs may be disruptive to our operations. For example, our workforce reductions could yield unanticipated consequences, such as turnover beyond planned reductions or increased difficulties in our day-to-day operations. Our workforce reductions could also harm our ability to attract and retain qualified personnel who are critical to our business. Any failure to attract or retain qualified personnel could prevent us from successfully executing key technical initiatives.

The COVID-19 pandemic could adversely impact our business, results of operations and financial condition.

The ongoing COVID-19 pandemic has dramatically impacted the global health and economic environment, including millions of confirmed cases and deaths, business slowdowns or shutdowns, labor shortages, supply chain challenges, changes in government requirements, regulatory challenges, inflationary pressures and market volatility. Although we have, to date, managed to continue most of our operations, we cannot predict the future course of events nor can we assure that this global pandemic, including its economic impact, will not have a material adverse impact on our business, results of operations and financial condition. The extent to which COVID-19 may impact us will depend on a variety of factors and future developments, which are highly uncertain and cannot be predicted with confidence, including the duration, scope and severity of the pandemic, the duration and extent of travel restrictions and social distancing in the United States and other countries, business closures or other business disruptions, including supply chain disruptions and labor shortages, and the effectiveness of actions taken in the United States and other countries to contain and treat COVID-19, including global vaccination efforts.

Public health actions undertaken globally in response to the COVID-19 pandemic, including quarantines, stay-at-home, executive and similar government orders and the prioritization of healthcare resources, have adversely impacted and could continue to adversely impact our business, results of operations and financial condition. As a result of these public health actions, we have experienced and continue to experience, and may in the future experience, disruptions that severely impact our business, clinical trials and preclinical studies, and operations, 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;
- 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; and
- 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.

As a result of the ongoing COVID-19 pandemic, our business, results of operations and preclinical and clinical development processes have been and may continue to be negatively impacted, including in connection with the ability of regulators to continue ensuring the timely review and approval of applications. During the COVID-19 public health emergency, a number of companies announced receipt of complete response letters due to the FDA's inability to complete required inspections for their applications. Our ability to conduct our business in the manner and on the timelines presently planned could have a material adverse impact on our business, results of operations and financial condition.

To the extent the ongoing 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 commercial sales, 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 product candidates, and our ability to raise additional capital to support our operations and to service our indebtedness. In addition, any recurrence or subsequent "wave" of COVID-19 cases, including those caused by new variants, could cause other widespread or more severe impacts depending on where infection rates are highest. While certain vaccines and treatments for COVID-19 have been authorized for use, some in emergency cases, there can be no assurance that such measures will halt or slow the progression of COVID-19 in a timely manner or at all.

Our future success depends on our ability to retain key employees, directors, consultants and advisors and to attract, retain and motivate qualified personnel.

We are highly dependent on the management, research and development, clinical, financial and business development expertise of our executive officers, our directors, our Management Committee as well as the other members of our scientific and clinical teams.

If we were to lose Dr. Kumar or any of our other executives or key personnel, we may not be able to find appropriate replacements on a timely basis. In addition, because certain of our employees provide a centralized source of support across multiple subsidiaries, the loss of any of these employees could negatively affect the operations of the affected subsidiaries, 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. We do not maintain “key person” insurance for any of our executives or employees. Recruiting and retaining qualified scientific and clinical personnel and, if we progress the development of our drug 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 our product candidates. 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.

Our reliance on a central team consisting of a limited number of employees who provide various administrative, research and development and other services across our organization, and on dedicated teams at the subsidiary level presents operational challenges that may adversely affect our business.

As of December 31, 2022, we had 392 employees. While we believe this structure enables us to reduce certain infrastructure costs, the small size of our central team may cause us to be unable to devote adequate personnel, time and resources to support the operations of all of our subsidiaries, including their research and development activities, employee recruiting and retention efforts and the management financial and accounting and reporting matters. From time to time, members of our central team may not have access to adequate information regarding aspects of the business and operations of our subsidiaries to sufficiently manage these affairs. Additionally, because our dedicated subsidiary-level employees and management are primarily incentivized at the subsidiary level, these employees and management team members may not be sufficiently incentivized to maximize the overall value of our entire organization. If our central team fails to provide adequate administrative, research and development or other services across our entire organization, or our subsidiary-level employees and management do not perform in a manner that aligns with the interests of our entire organization, our business, financial condition and results of operations could be harmed.

Changes in funding for, or disruptions to the operations of, the FDA, the SEC and other government agencies could hinder their ability to hire and retain key leadership and other personnel, prevent new products 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.

Inadequate funding for the FDA, the SEC and other government agencies, including from government shut downs, or other disruptions to these agencies' operations, could hinder their ability to hire and retain key leadership and other personnel, prevent new products and services from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal business 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 products 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, the availability of personnel and other resources in light of governmental "stay at home" orders in response to the COVID-19 pandemic, and statutory, regulatory and policy changes. Average review times at the agency have fluctuated in recent years as a result. 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.

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, including for 35 days beginning on December 22, 2018, 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. Since March 2020, when foreign and domestic inspections of facilities were largely placed on hold, the FDA has been working to resume pre-pandemic levels of inspection activities, including routine surveillance, bioresearch monitoring and pre-approval inspections. 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, and the FDA does not determine a remote interactive evaluation to be adequate, the FDA has stated that it generally intends to issue, depending on the circumstances, a complete response letter or defer action on the application until an inspection can be completed. Regulatory authorities outside the United States may adopt similar restrictions or other policy measures in response to the COVID-19 pandemic and may experience delays in their regulatory activities. If a prolonged government shutdown or disruption to the operations of the FDA 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 or disruption to the operations of the USPTO could prevent the timely review of our patent applications, which could delay the issuance of any U.S. patents to which we might otherwise be entitled. Future government shutdowns and similar events could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

We will need to expand our organization and we may experience difficulties in managing this growth, which could disrupt our operations.

As of December 31, 2022, we had 392 full-time employees across all of our companies. 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 commercialization of our product candidates, if approved and development of additional product 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 product candidates if approved, and compete effectively will depend, in part, on our ability to effectively manage any future growth.

Because we have multiple programs and product candidates in our development pipeline and are pursuing a variety of target indications and treatment modalities, we may expend our limited resources to pursue a particular product candidate and fail to capitalize on development opportunities or product candidates that may be more profitable or for which there is a greater likelihood of success.

We focus on the development of product candidates to address Mendelian diseases and genetically driven cancers, regardless of the treatment modality or the particular target indication within this space. Because we have limited financial and personnel resources, we may forego or delay pursuit of opportunities with potential target indications or product candidates that later prove to have greater commercial potential than our current and planned development programs and product candidates. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and other future product candidates for specific indications may not yield any commercially viable future product candidates. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may be required to relinquish valuable rights to that product 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 product candidates.

Additionally, we may pursue additional in-licenses or acquisitions of development-stage assets or programs, which entails additional risk to us. Identifying, selecting and acquiring promising product 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 product 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 products, we may spend material amounts of our capital and other resources evaluating, acquiring and developing products 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 product candidates that we may develop.

We face an inherent risk of product liability exposure related to the testing of product candidates in human clinical trials in the commercial sales of approved medicines. If we cannot successfully defend ourselves against claims that our product candidates or medicines caused injuries, we could incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for any product candidates or medicines;
- 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 successfully commercialize our product candidates or medicines.

Although we maintain product liability insurance, including coverage for clinical trials that we sponsor and for our commercial product sales, 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 as we commercialize product candidates that may be approved. The market for insurance coverage is increasingly expensive, and the costs of insurance coverage will increase as our clinical programs and commercialization efforts 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.

Our 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. 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 obtain FDA approval of our product candidates and begin commercializing those products in the United States, we believe that 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. We have adopted a code of business conduct and ethics applicable to our employees and directors, but 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.

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.

We are conducting clinical trials internationally through a global CRO, and our business strategy incorporates potential international expansion to target patient populations outside the United States. If we receive regulatory approval for and commercialize any of our product 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 products 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 products, and exposure to foreign currency exchange rate fluctuations;

- natural disasters, political and economic instability, including wars, terrorism, and political unrest, outbreak of disease (such as the COVID-19 pandemic), 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, 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.

If we fail to maintain an effective system of disclosure controls and internal control over financial reporting, our ability to produce timely and accurate financial statements or comply with applicable regulations could be impaired, which could negatively affect the price of our common stock.

As a public company, we are required to maintain internal control over financial reporting and to report any material weaknesses in such internal controls. The Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, requires that we evaluate and determine the effectiveness of our internal control over financial reporting and, pursuant to Section 404(b) of the Sarbanes Oxley Act, or Section 404, beginning with our second annual report following our IPO, provide a management report on internal control over financial reporting. In addition, we are required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. Any failure to develop or maintain effective controls, or any difficulties encountered in their implementation or improvement, could harm our results of operations, cause us to fail to meet our reporting obligations, result in a restatement of our financial statements for prior periods, or adversely affect the results of management evaluations and independent registered public accounting firm audits of our internal control over financial reporting that we will eventually be required to include in our periodic reports that will be filed with the SEC.

In addition, to the extent we acquire or establish additional consolidated subsidiaries and VIEs, the financial statements of such entities may not be initially prepared by us, and we will not have direct control over their financial statement preparation. As a result, we will, for our financial reporting, depend on what these entities report to us, which could result in our adding monitoring and audit processes, and increase the difficulty of implementing and maintaining adequate controls over our financial processes and reporting in the future, which could lead to delays in our external reporting. In particular, this may occur where we are establishing such entities with partners that do not have sophisticated financial accounting processes in place, or where we are entering into new relationships at a rapid pace, straining our integration capacity. We have in the past identified material weaknesses in our internal control over financial reporting. Although these material weaknesses were remediated, we could identify additional material weaknesses in the future, and a combination of significant deficiencies could result in a material weakness. If we identify any such additional material weaknesses or are required to restate previously issued financial statements for any additional periods, our reputation could be impaired which could cause a loss of investor confidence and adversely materially affect our business, operating results and financial condition. Additionally, if we do not receive the information from the consolidated subsidiaries or controlled VIEs on a timely basis, it could cause delays in our external reporting. Ineffective disclosure controls and procedures and internal controls over financial reporting could also cause investors to lose confidence in our reported financial and other information, which would likely have a negative effect on the trading price of our common stock.

Historically, we have relied upon and expect to continue to rely upon third-party contracted service providers to assist with our financial reporting. The process of designing, implementing and maintaining the internal control over financial reporting required to comply with the Sarbanes-Oxley Act is time consuming, costly, and complicated. If we are unable to assert that our internal control over financial reporting is effective or when required in the future, if our independent registered public accounting firm issues an adverse opinion on the effectiveness of our internal control over financial reporting, investors may lose confidence in the accuracy and completeness of our financial reports, the market price of our common stock could be adversely affected and we could become subject to investigations or sanctions by the stock exchange on which our securities are listed, the SEC, or other regulatory authorities, which could require additional financial and management resources.

We do not expect that our disclosure controls or our internal control over financial reporting will prevent all errors and all fraud.

A control system, no matter how well designed and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. Further, the design of a control system must reflect the fact that there are resource constraints, and the benefits of controls must be considered relative to their costs. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that all control issues and instances of fraud, if any, have been detected. These inherent limitations include the realities that judgments in decision-making can be faulty, and that breakdowns can occur because of a 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 management override of the controls. The design of any system of controls is also based in part upon certain assumptions about the likelihood of future events, and there can be no assurance that any design will succeed in achieving its stated goals under all potential future conditions; over time, controls may become inadequate because of changes in conditions, or the degree of compliance with policies or procedures may deteriorate. Because of the inherent limitations in a cost-effective control system, misstatements due to error or fraud may occur and may not be detected.

Risks Related to Our Indebtedness

We have incurred a significant amount of debt and may in the future incur additional indebtedness. Servicing our debt requires a significant amount of cash, and we may not have sufficient cash flow from our business to pay our substantial debt.

As of December 31, 2022, we and our subsidiaries had total consolidated indebtedness of $1.7 billion, including $550.0 million of indebtedness outstanding under our unsecured 2.50% Convertible Senior Notes due 2027, or the 2027 Notes, $747.5 million of indebtedness outstanding under our 2.25% Convertible Senior Notes due 2029, or the 2029 Notes, and $445.2 million of indebtedness under our loan agreement by and among U.S. Bank National Association, certain lenders, BridgeBio as borrower, and certain subsidiaries of BridgeBio as guarantors, or the Loan Agreement. Subject to the limitations in the terms of our existing and future indebtedness, we and our subsidiaries may incur additional indebtedness, secure existing or future indebtedness, or refinance our indebtedness. We may be required to use a substantial portion of our cash flows from operations to pay interest and principal on our indebtedness. Our ability to make scheduled payments of the principal of, to pay interest on or to refinance our indebtedness, depends on our future performance and our ability to generate sufficient cash flow from our operations, which are subject to economic, financial, competitive and other factors beyond our control. Such payments will reduce the funds available to us for working capital, capital expenditures, and other corporate purposes and limit our ability to obtain additional financing for working capital, capital expenditures, expansion plans, and other investments, which may in turn limit our ability to implement our business strategy, heighten our vulnerability to downturns in our business, the industry, or in the general economy, limit our flexibility in planning for, or reacting to, changes in our business and the industry, and prevent us from taking advantage of business opportunities as they arise. Additionally, if we are unable to generate sufficient cash flow to service our indebtedness and fund our operations, we may be required to adopt one or more alternatives, such as selling assets, restructuring debt or obtaining additional equity capital on terms that may be onerous or highly dilutive. We may not be able to engage in any of these activities or engage in these activities on desirable terms, which could result in a default on our debt obligations.

We have incurred indebtedness under our convertible senior notes and are party to a loan and security agreement that contain operating and financial covenants that may restrict our business and financing activities.

In March 2020, we issued the 2027 Notes, pursuant to which we pay interest semiannually in arrears at a rate of 2.50% per year. The 2027 Notes will mature on March 15, 2027 unless earlier converted or repurchased, at which time we will settle any conversions of the 2027 Notes in cash, shares of our common stock or a combination thereof, at our election. In January and February 2021, we issued the 2029 Notes, pursuant to which we pay interest semiannually in arrears at a rate of 2.25% per year. The 2029 Notes will mature on February 1, 2029 unless earlier converted or repurchased, at which time we will settle any conversions of the 2029 Notes in cash, shares of our common stock or a combination thereof, at our election. Under certain circumstances, the holders of the 2027 Notes and the 2029 Notes, or collectively, the Notes, may require us to repay all or a portion of the principal and interest outstanding under the Notes in cash prior to their respective maturity dates, which could have an adverse effect on our financial results.

In November 2021, we entered into the Loan Agreement, pursuant to which we were extended term loans in an aggregate principal amount of up to $750.0 million, comprised of (i) a tranche 1 advance of $450.0 million, or the Tranche 1 Advance, and (ii) a tranche 2 advance of $300.0 million, or the Tranche 2 Advance, or collectively, the Term Loan Advances. The Tranche 1 Advance was funded on November 17, 2021. In May 2022, we amended the Loan Agreement to, among other things, reduce the Tranche 2 Advance to $100.0 million. In November 2022, we further amended the Loan Agreement to, among other things, terminate the ability for us to draw down the Tranche 2 Advance. The term loans mature on November 16, 2026. The Loan Agreement may restrict our ability, among other things, to:

- sell, transfer or otherwise dispose of any of our business or property, subject to limited exceptions;
- make material changes to our business;
- enter into transactions resulting in significant changes to the voting control of our stock;
- make certain changes to our organizational structure;
- consolidate or merge with other entities or acquire other entities;
- incur additional indebtedness or create encumbrances on our assets;
- pay dividends, or make distributions on and, in certain cases, repurchase our stock;
- enter into transactions with our affiliates;
- repay subordinated indebtedness; or
- make certain investments.

In addition, we are required under the Loan Agreement to comply with various operating covenants and default clauses that may restrict our ability to finance our operations, engage in business activities or expand or fully pursue our business strategies. A breach of any of these covenants or clauses could result in a default under the Loan Agreement, which could cause all of the outstanding indebtedness under the facility to become immediately due and payable.

Under the Loan Agreement, we also have an obligation to pledge our equity interests in our subsidiaries. In addition, certain of our non-operating subsidiaries, which are subsidiaries other than those predominantly involved in advancing our development programs, are also obligated to enter into a joinder agreement, whereby they are also required to comply with the terms of the Loan Agreement. Any breach by us, or any event of default under, our Loan Agreement could result in a material adverse effect on our business, financial condition and operating results.

The conditional conversion feature of the Notes, if triggered, may adversely affect our financial condition and operating results.

In the event the conditional conversion feature of the Notes is triggered, holders of the Notes will be entitled to convert the notes at any time during specified periods at their option. If one or more holders elect to convert their Notes, unless we elect to satisfy our conversion obligation by delivering solely shares of our common stock (other than paying cash in lieu of delivering any fractional share), we would be required to settle a portion or all of our conversion obligation through the payment of cash, which could adversely affect our liquidity. In addition, even if holders do not elect to convert their Notes, we could be required under applicable accounting rules to reclassify all or a portion of the outstanding principal of the notes as a current rather than long-term liability, which would result in a material reduction of our net working capital.

Risks Related to Our Need for Additional Capital

We will 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 our product development and commercialization efforts.

Developing and commercializing biopharmaceutical products is expensive and time-consuming, and we expect to require substantial additional capital to conduct research, preclinical testing and human studies, may establish pilot scale and commercial scale manufacturing processes and facilities, and establish and develop quality control, regulatory, marketing, sales and administrative capabilities to support our existing programs and pursue potential additional 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 commercialization of any future product candidates we may identify.

As of December 31, 2022, we had working capital of $427.4 million, of which cash, cash equivalents and marketable securities amounted to $428.3 million, restricted cash amounted to $37.9 million, and investment in equity securities amounted to $43.7 million. We expect that our cash and cash equivalents, marketable securities, restricted cash and investment in equity securities will be sufficient to fund our operations through at least the next 12 months from the date of this report. However, our operating plan may change as a result of many factors currently unknown to us, including the effects of the COVID-19 pandemic on our research and development and commercialization activities, and we may need to seek additional funds sooner than planned, through public or private equity or debt financings or other sources, such as strategic collaborations or license and development agreements. Any 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 product candidates that we may identify and pursue. Moreover, such financing may result in dilution to stockholders, imposition of debt covenants and repayment obligations, or other restrictions that may affect our business. In addition, we may seek additional capital due to favorable market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans.

Our future funding requirements will depend on many factors, including, but not limited to:

- the time and cost necessary to complete ongoing and planned clinical trials, including our ongoing Phase 3 clinical trial of acoramidis, our ongoing Phase 2 and planned Phase 3 clinical trials of low-dose infigratinib, our ongoing Phase 2 clinical trial of BBP-631 and our ongoing Phase 3 clinical trial of encaleret;
- the time and cost necessary to pursue regulatory approvals for our product candidates, and the costs of post-marketing studies that could be required by regulatory authorities;

- the progress, timing, scope and costs of our nonclinical studies, preclinical studies, clinical trials and other related activities, including the ability to enroll patients in a timely manner, for the ongoing and planned clinical trials set forth above, and potential future clinical trials;
- the costs of obtaining adequate clinical and commercial supplies of raw materials and drug products for our product candidates, including gene therapies such as BBP-631, and BBP-812 and any other product candidates we may identify and develop;
- our ability to successfully identify and negotiate acceptable terms for third-party supply and contract manufacturing agreements with CMOs;
- our ability to successfully commercialize any product candidates that may be approved;
- the manufacturing, selling and marketing costs associated with any product candidates that may be approved, including the cost and timing of expanding our internal sales and marketing 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 any approved products, including the sales price and the availability of adequate third-party reimbursement;
- the cash requirements of any future acquisitions or discovery of product candidates;
- the time and cost necessary to respond to technological and market developments;
- the costs of acquiring, licensing or investing in intellectual property rights, products, product candidates and businesses;
- our ability to continue to discover and develop additional product candidates, and the time and costs associated with identifying additional product candidates;
- our ability to attract, hire and retain qualified personnel; and
- the costs of maintaining, expanding and protecting our intellectual property portfolio.

Additional funds may not be available when we need them, on terms that are acceptable, 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 commercialization of any product candidates 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 stockholders, restrict our operations or require us to relinquish rights to current product candidates or to any future product candidates on unfavorable terms.

We may seek additional capital through any number of available sources, including, but not limited to, public and private equity offerings, debt financings, strategic partnerships and alliances and licensing arrangements. We, and indirectly, our stockholders, will 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 raise additional capital through the sale of additional equity or debt securities, your ownership interest will be diluted, and the terms may include liquidation or other preferences that adversely affect your rights as a stockholder. 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 product candidates, or grant licenses or other rights on unfavorable terms.

In addition, if one of our subsidiaries raises funds through the issuance of equity securities to third parties, our stockholders' deficit interests in such subsidiary could be substantially diminished. If one of our subsidiaries raises additional funds through collaboration and licensing arrangements, it may be necessary to relinquish some rights to our technologies or our product candidates or grant licenses on terms that are not favorable to us.

If we engage in other acquisitions or strategic partnerships, this may increase our capital requirements, dilute our stockholders, 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 products, 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 stockholders;
- assimilation of operations, intellectual property, product candidates of an acquired company, including difficulties associated with integrating new personnel;
- the diversion of our management's attention from our existing product programs and initiatives in pursuing such an acquisition or strategic partnership;
- difficulties in retaining key employees and 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 products or product candidates and regulatory approvals; and
- our inability to generate revenue from acquired intellectual property, technology and/or products 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, any of which could have a material adverse effect on our business, prospects, financial condition and results of operations. For example, the Eidos Merger resulted in a reduction of our cash and dilutive issuances of our equity securities to the former Eidos stockholders. Any similar transactions in the future that require us to provide cash or stock consideration could harm our financial condition and negatively impact our existing stockholders.

Recent volatility in capital markets and lower market prices for our securities may affect our ability to access new capital through sales of shares of our common stock or issuance of indebtedness, which may harm our liquidity, limit our ability to grow our business, pursue acquisitions or improve our operating infrastructure and restrict our ability to compete in our markets.

Our operations consume substantial amounts of cash, and we intend to continue to make significant investments to support our business growth, respond to business challenges or opportunities, develop new product candidates, retain or expand our current levels of personnel, improve our existing product candidates, enhance our operating infrastructure, and potentially acquire complementary businesses and technologies. Our future capital requirements may be significantly different from our current estimates and will depend on many factors, including the need to:

- finance unanticipated working capital requirements;
- continue the research and development of our existing product candidates and develop or enhance our technological infrastructure;
- pursue acquisitions, in-licenses or other strategic relationships; and
- respond to competitive pressures.

Accordingly, we may need to pursue equity, debt or other financings to meet our capital needs. With uncertainty in the capital markets and other factors, such financing may not be available on terms favorable to us or at all. If we raise additional funds through further issuances of equity or convertible debt securities, our existing stockholders could suffer significant dilution, and any new equity securities we issue could have rights, preferences, and privileges superior to those of holders of our common stock. In addition, any debt financing secured by us may subject us to fixed payment obligations and covenants limiting or restricting our ability to take specific actions such as capital-raising activities, incurring additional debt, making capital expenditures or declaring dividends, and could involve additional restrictive covenants relating to our capital-raising activities and other financial and operational matters, which may make it more difficult for us to obtain additional capital and to pursue business opportunities, including potential acquisitions. If we raise additional capital through marketing and distribution arrangements or other collaborations, or strategic alliances or licensing arrangements with third parties, we may have to relinquish certain valuable rights to our product candidates, technologies, future revenue streams or research programs or grant licenses on terms that may not be favorable to us. Furthermore, recent increases in interest rates could affect our ability to obtain working capital through borrowings such as bank credit lines and public or private sales of debt securities, which may result in lower liquidity, reduced working capital and other adverse impacts on our business. If we are unable to obtain adequate financing or financing on terms satisfactory to us, we could face significant limitations on our ability to invest in our operations and otherwise suffer harm to our business.

Risks Related to Our Common Stock

The market price of our common stock has been and may be highly volatile, and purchasers of our common stock could incur substantial losses.

The market price of our common stock has been and is likely to continue to be volatile. Our stock price has been and may be subject to wide fluctuations in response to a variety of factors, including the following:

- adverse results or delays in our preclinical studies or clinical trials;
- reports of AEs or other negative results in clinical trials of third parties' product candidates that target our product candidates' target indications;
- inability for us to obtain additional funding, or to service our existing debt obligations, on reasonable terms or at all;
- any delay in filing an IND, BLA or NDA for our product 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 our product candidates;
- the termination of, or any other failure to develop successfully and commercialize our product candidates;
- announcements we make regarding our current product candidates, acquisition of potential new product candidates and companies and/or in-licensing;
- the termination of, or any other failure to maintain our existing license arrangements or enter into new licensing and collaboration agreements;
- failure by us or our licensors to prosecute, maintain or enforce our intellectual property rights;
- changes in laws or regulations applicable to future products;
- inability to obtain adequate clinical or commercial supply for our product 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 our product candidates;
- regulatory approval or commercialization of new products 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;
- the perception of the pharmaceutical industry by the public, legislatures, regulators and the investment community;
- announcements of significant acquisitions, strategic partnerships, joint ventures or capital commitments by us, our strategic collaboration partners or our competitors;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- additions or departures of our key scientific or management personnel;
- significant lawsuits, including patent or stockholder litigation, against us;
- changes in the market valuations of similar companies;
- sales or potential sales of substantial amounts of our common stock;
- trading volume of our common stock;
- acts of war or periods of widespread civil unrest, including the increasingly volatile global economic conditions resulting from the conflicts in Ukraine;
- general economic and market conditions, including inflationary pressures and stock market volatility; and
- continued increases in interest rates that increase the cost of any potential new indebtedness.

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, including the effects of the COVID-19 pandemic, and the ongoing conflict in Ukraine, and global economic conditions on the global economy, may negatively affect the market price of our common stock, regardless of our actual operating performance.

We have in the past been, and could be subject to securities class action litigation and other types of stockholder litigation.

The stock market in general, and The Nasdaq Global Market and biotechnology companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. In the past, securities class action litigation has often been instituted against companies following periods of volatility in the market price of a company's securities. We could also be subject to other types of litigation, which may involve claims of breach of fiduciary duties by our directors or officers for misuse/mismanagement of company assets/resources or conflicts of interest. Any such litigation, if instituted, could result in substantial costs and a diversion of management's attention and resources, which would harm our business, operating results, or financial condition. Additionally, the dramatic increase in the cost of directors' and officers' liability insurance may cause us to opt for lower overall policy limits or to forgo insurance that we may otherwise rely on to cover significant defense costs, settlements, and damages awarded to plaintiffs.

Future sales and issuances of our common stock or rights to purchase common stock, including pursuant to our equity incentive plans, would result in additional dilution of the percentage ownership of our stockholders and could cause our stock price to fall.

We will need additional capital in the future to continue our planned operations. To the extent we raise additional capital by issuing equity securities, our stockholders may experience substantial dilution. We may sell common stock, convertible securities or other equity securities in one or more transactions at prices and in a manner we determine from time to time. If we sell common stock, convertible securities or other equity securities in more than one transaction, investors may be materially diluted by subsequent sales. These sales may also result in material dilution to our existing stockholders, and new investors could gain rights superior to our existing stockholders.

Pursuant to our 2021 Amended and Restated Stock Option and Incentive Plan, or the A&R 2021 Plan, we are authorized to grant stock options and other stock-based awards to our employees, directors and consultants. In addition, pursuant to our 2019 Inducement Equity Plan, we are authorized to grant stock options and other stock-based awards to prospective officers and employees who are not currently employed by us or one of our subsidiaries. If our board of directors, or the Board of Directors, elects in the future to increase the number of shares available for future grant and, in the case of the A&R 2021 Plan, if our stockholders approve of any such further increase, our stockholders may experience additional dilution, and our stock price may fall.

Any sales of a significant portion of our total outstanding shares into the market could cause the market price of our common stock to decline significantly.

Sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales or the perception in the market that the holders of a large number of shares of common stock intend to sell shares, could reduce the market price of our common stock.

Shares of unvested restricted stock and common stock issued and outstanding as of the 2019 Reorganization will become available for sale immediately upon the vesting of such shares. Shares issued upon the exercise of stock options outstanding under our equity incentive plans or pursuant to future awards granted under those plans will become available for sale in the public market to the extent permitted by the provisions of applicable vesting schedules, any applicable market standoff agreement, and Rule 144 and Rule 701 under the Securities Act of 1933, as amended, or the Securities Act.

Certain holders of our common stock have rights, subject to conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. In July 2020, we filed a registration statement on Form S-3ASR that became effective automatically upon filing. Pursuant to this registration statement, we were authorized to issue up to $350.0 million in common stock in sales deemed to be an "at the market offering" as defined by the Securities Act and, so long as we qualify as a "well-known seasoned issuer" as defined in Rule 405 of the Securities Act, an unlimited amount of shares of our common stock, preferred stock, debt securities, warrants and/or units. In July 2020, we filed a registration statement on Form S-3ASR, or the Selling Stockholder Form S-3, relating to the offer and resale from time to time by certain of our stockholders, of up to an aggregate of 65,121,374 shares of our common stock. In February 2021, one of our stockholders completed a sale of 3,450,000 shares of our common stock in an underwritten public offering pursuant to the Selling Stockholder Form S-3. We may also file registration statements in the future that register a substantial number of shares of our common stock where if any additional shares are sold pursuant to these registration statements, or if it is perceived that they will be sold, in the public market, the market price of our common stock could decline. We have also filed registration statements on Form S-8 registering the issuance of shares of common stock issued or reserved for future issuance under our equity compensation and equity inducement plans. Shares registered under these registration statements on Form S-8 can be freely sold in the public market upon issuance and once vested, subject to volume limitations applicable to affiliates. In addition, certain of our executive officers, employees and affiliates have established or may in the future establish programmed selling plans under Rule 10b5-1 of the Securities Exchange Act of 1934, as amended, for the purpose of effecting sales of our common stock. If any of these additional shares are sold, or if it is perceived that they will be sold, in the public market, the market price of our common stock could decline.

If securities analysts do not publish research or reports about our business or if they publish negative evaluations of our stock, the price of our stock could decline.

The trading market for our common stock relies in part on the research and reports that industry or financial analysts publish about us or our business. If one or more of the analysts covering our business downgrade their evaluations of our stock, the price of our stock could decline. If one or more of these analysts cease to cover our stock, we could lose visibility in the market for our stock, which in turn could cause our stock price to decline.

Our principal stockholders and certain members of our management own a significant percentage of our stock and will be able to exert significant control over matters subject to stockholder approval.

Based upon our common stock outstanding as of December 31, 2022, our beneficial stockholders, directors, and executive officers beneficially own 58.4% of our outstanding common stock. These stockholders will have the ability to influence us through their ownership positions. These stockholders may be able to determine all matters requiring stockholder approval. For example, these stockholders, acting together, may be able to control elections of directors, amendments of our organizational documents, or approval of any merger, sale of assets, or other major corporate transaction. In turn, this may have an adverse effect on the market price of our common stock. This may prevent or discourage unsolicited acquisition proposals or offers for our common stock that you may believe are in your best interest as one of our stockholders. In certain circumstances, these stockholders' interests as stockholders may differ or even conflict with the interests of our stockholders.

Provisions in our amended and restated certificate of incorporation and amended and restated bylaws, as well as provisions of Delaware law, could make it more difficult for a third party to acquire us or increase the cost of acquiring us, even if doing so would benefit our stockholders or remove our current management.

Our amended and restated certificate of incorporation and amended and restated bylaws and Delaware law contain provisions that may have the effect of delaying or preventing a change in control of us or changes in our management. Our amended and restated certificate of incorporation and amended and restated bylaws include provisions that:

- authorize "blank check" preferred stock, which could be issued by our Board of Directors without stockholder approval and may contain voting, liquidation, dividend and other rights superior to our common stock;
- create a classified Board of Directors whose members serve staggered three-year terms;
- specify that special meetings of our stockholders can be called only by our Board of Directors or stockholders holding at least 25% of our outstanding voting stock;
- prohibit stockholder action by written consent;
- establish an advance notice procedure for stockholder approvals to be brought before an annual meeting of our stockholders, including proposed nominations of persons for election to our Board of Directors;
- provide that vacancies on our Board of Directors may be filled only by a majority of directors then in office, even if less than a quorum, or by the holders of a majority of the outstanding shares of capital stock then entitled to vote at an election of directors;
- specify that no stockholder is permitted to cumulate votes at any election of directors;
- expressly authorize our Board of Directors to modify, alter or repeal our amended and restated bylaws; and
- require supermajority votes of the holders of our common stock to amend specified provisions of our amended and restated certificate of incorporation and amended and restated bylaws.

These provisions, alone or together, could delay or prevent hostile takeovers and changes in control or changes in our management.

In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which limits the ability of stockholders owning in excess of 15% of our outstanding voting stock to merge or combine with us. Any provision of our amended and restated certificate of incorporation or amended and restated bylaws or Delaware law that has the effect of delaying or deterring a change in control could limit the opportunity for our stockholders to receive a premium for their shares of our common stock, and could also affect the price that some investors are willing to pay for our common stock.

Our amended and restated bylaws designate specific courts as the exclusive forum for certain litigation that may be initiated by our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us.

Pursuant to our amended and restated bylaws, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for any state law claim for (i) any derivative action or proceeding brought on our behalf; (ii) any action asserting a claim of breach of or based on a fiduciary duty owed by any of our current or former directors, officers or employees to us or our stockholders; (iii) any action asserting a claim against us arising pursuant to any provision of the Delaware General Corporation Law or our amended and restated certificate of incorporation or amended and restated bylaws; (iv) any action to interpret, apply, enforce or determine the validity of our amended and restated certificate of incorporation or amended and restated bylaws; or (v) any action asserting a claim governed by the internal affairs doctrine of the State of Delaware. Our amended and restated bylaws further provide that, unless we consent in writing to the selection of an alternative forum, the federal district courts of the United States will be the sole and exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act. The forum selection clauses in our amended and restated bylaws may limit our stockholders' ability to obtain a favorable judicial forum for disputes with us.

Our operating results may fluctuate significantly, which makes our future operating results difficult to predict and could cause our operating results to fall below expectations or our guidance.

Our quarterly and annual operating results may fluctuate significantly in the future, which makes it difficult for us to predict our future operating results. Our operating results may fluctuate due to a variety of factors, many of which are outside of our control and may be difficult to predict, including but not limited to the following:

- the timing, results and cost of, and level of investment in, our clinical development activities for our current product candidates and any other product candidates we may identify and pursue, which may change from time to time;
- the cost of manufacturing our current product candidates and the related materials or other product candidates that we may identify, which may vary depending on the quantity of production and the terms of agreements with manufacturers;
- our ability to conduct our ongoing and planned clinical trials in accordance with our current plans and to obtain regulatory approval for our current product candidates or other product candidates that we may identify, and the timing and scope of any such approvals we may receive;
- the timing and success or failure of clinical trials for competing product candidates, or any other change in the competitive landscape of our industry, including consolidation among our competitors or partners;
- expenditures that we or will or may incur to acquire or develop additional product candidates and technologies;
- our ability to attract, hire and retain qualified personnel;
- the level of demand for our current product candidates or other product candidates that we may identify, should they receive approval, which may vary significantly;
- future accounting pronouncements or changes in our accounting policies;
- the risk/benefit profile, cost and reimbursement policies with respect to our current product candidates or other product candidates that we may identify, if approved, and existing and potential future drugs that compete with our product candidates;
- the success of our restructuring initiative; and
- the changing and volatile U.S., European and global economic environments, including volatility associated with the global COVID-19 pandemic.

The cumulative effects of these factors could result in large fluctuations and unpredictability in our quarterly and annual operating results. As a result, comparing our operating results on a period-to-period basis may not be meaningful. This variability and unpredictability could also result in our failing to meet the expectations of industry or financial analysts or investors for any period. If our operating results fall below the expectations of analysts or investors or below any forecasts we may provide to the market, or if the forecasts we provide to the market are below the expectations of analysts or investors, the price of our common stock could decline substantially.

Our future ability to utilize our net operating loss carryforwards and certain other tax attributes may be limited.

We have incurred substantial losses during our history and we do not expect to become profitable in the near future and we may never achieve profitability. To the extent that we continue to generate taxable losses, unused losses will carry forward indefinitely if not utilized, subject to expiration of such carryforwards in the case of federal net operating loss carryforwards generated prior to 2018. In addition, under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, or the Code, and corresponding provisions of state law, if a corporation undergoes an "ownership change," generally defined as a greater than 50 percentage point change (by value) in its equity ownership over a three-year period, the corporation's ability to use its pre-change net operating loss carryforwards, or NOLs, and other pre-change tax attributes to offset its post-change income or taxes may be limited. Our existing net operating losses or credits may be subject to limitations arising from previous ownership changes and if we undergo future ownership changes, many of which may be outside of our control, our ability to utilize our net operating losses or credits could be further limited by Sections 382 and 383 of the Code. Accordingly, we may not be able to utilize a material portion of our net operating losses or credits. In addition, the amount of post-2017 NOLs that we are permitted to deduct in taxable years beginning after December 31, 2022 is limited to 80% of our taxable income in such year.

Changes in tax law may adversely affect us or our investors.

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. For example, under Section 174 of the Code, in taxable years beginning after December 31, 2021, expenses that are incurred for research and development in the U.S. will be capitalized and amortized, which may have an adverse effect on our cash flow. In recent years, many such changes have been made, and changes are likely to continue to occur in the future. It cannot be predicted whether, when, in what form or with what effective dates tax laws, regulations and rulings may be enacted, promulgated or issued, which could result in an increase in our or our shareholders' tax liability or require changes in the manner in which we operate in order to minimize or mitigate any adverse effects of changes in tax law.

We have never and do not currently intend to pay dividends on our common stock, and, consequently, our stockholders' ability to achieve a return on their investment will depend on appreciation in the price of our common stock.

We have never paid cash dividends on any of our capital stock and do not currently intend to pay any cash dividends on our common stock for the foreseeable future. In addition, pursuant to the Loan Agreement, we are not permitted to declare or pay any cash dividends or make cash distributions on any class of our capital stock or any other equity interest, except in limited circumstances. We currently intend to invest our future earnings, if any, to fund our growth. Therefore, you are not likely to receive any dividends on your common stock for the foreseeable future. Since we do not intend to pay dividends, your ability to receive a return on your investment will depend on any future appreciation in the market value of our common stock. There is no guarantee that our common stock will appreciate or even maintain the price at which our holders have purchased it.

We have incurred and will continue to incur significant costs as a result of operating as a public company, and our management is required to devote substantial time to new compliance initiatives. We are subject to financial reporting and other requirements for which our accounting and other management systems and resources may not be adequately prepared.

As a public company, we incur significant legal, accounting and other expenses that we did not incur as a private company. We are subject to the reporting requirements of the Exchange Act, which requires, among other things, that we file with the SEC, annual, quarterly and current reports with respect to our business and financial condition and that of our consolidated subsidiaries. In addition, the Sarbanes-Oxley Act, as well as rules subsequently adopted by the SEC and Nasdaq to implement provisions of the Sarbanes-Oxley Act, impose significant requirements on public companies, including requirements to file annual, quarterly, and event driven reports with respect to our business and financial condition, and requirements for the establishment and maintenance of effective disclosure and financial controls and changes in corporate governance practices.

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. Our compliance with Section 404, including the auditor attestation requirement, necessitates that we incur substantial accounting expense and expend significant management efforts. We will 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 that neither we nor our independent registered public accounting firm will be able to conclude within the prescribed timeframe 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.

Further, in July 2010, the Dodd-Frank Wall Street Reform and Consumer Protection Act, or the Dodd-Frank Act, was enacted. There are significant corporate governance and executive compensation-related provisions in the Dodd-Frank Act that require the SEC to adopt additional rules and regulations in these areas such as “say on pay” and proxy access. Stockholder activism, the current political environment and the current high level of government intervention and regulatory reform may lead to substantial new regulations and disclosure obligations, which may lead to additional compliance costs and impact the manner in which we operate our business in ways we cannot currently anticipate.

Additionally, there continues to be public interest and increased legislative pressure related to environmental, social and governance, or ESG, activities of public companies. We risk negative stockholder reaction, including from proxy advisory services, as well as damage to our brand and reputation, if we do not act responsibly in a number of key areas, including diversity and inclusion, environmental stewardship, support for local communities, corporate governance and transparency and considering ESG and human capital factors in our operations. There is a growing number of states requiring organizations to report their board composition as well or mandating gender diversity and representation from underrepresented communities, including New York and California.

We expect the rules and regulations applicable to us as a public company to substantially increase our legal and financial compliance costs and to make some activities more time-consuming and costly. If these requirements divert the attention of our management and personnel from other business concerns, they could have a material adverse effect on our business, financial condition and results of operations. The increased costs will decrease our net income or increase our net loss, and may require us to reduce costs in other areas of our business, including our subsidiaries. For example, our status as a public Company makes it more difficult and more expensive for us to obtain director and officer liability insurance and we may be required to incur substantial costs to maintain the level of coverage that we believe is appropriate for a public Company. We cannot predict or estimate the amount or timing of additional costs we may incur to comply with ongoing requirements or respond to any changes of these requirements. The impact of these requirements could also make it more difficult for us to attract and retain qualified persons to serve on our Board of Directors, our board committees or as executive officers.

Our business could be negatively impacted by corporate citizenship and environmental, social and corporate governance, or ESG, matters and/or our reporting of such matters.

There is an increasing focus from certain investors, consumers, and other stakeholders concerning corporate citizenship and sustainability matters. We could be perceived as not acting responsibly in connection with these matters. Our business could be negatively impacted by such matters. Any such matters, or related corporate citizenship and sustainability matters, could have a material adverse effect on our business.

Risks Following the Eidos Merger

We may be subject to litigation in connection with the Eidos Merger.

Lawsuits have been filed against us, certain of our subsidiaries, Eidos and Eidos' directors in connection with the Eidos Merger. Moreover, additional lawsuits may be filed against us, Eidos, our subsidiaries or our respective directors or executive officers in connection with the Eidos Merger and the related transactions, and while it is not possible to accurately predict future litigation and its impact, it is possible that such suits could result in substantial costs to BridgeBio and Eidos.

The defense or settlement of any legal proceedings or future litigation could be time-consuming and expensive, divert the attention of BridgeBio management and/or Eidos management away from their regular business, and, if any one of these legal proceedings or any future litigation is adversely resolved against either BridgeBio or Eidos, could have a material adverse effect on their respective financial condition, results of operations or liquidity.

General Risk Factors

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 products. 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 that 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 production efforts. Our failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Unfavorable global economic conditions 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 due to high levels of unemployment (particularly as a result of the COVID-19 pandemic), underemployment or the repeal of certain provisions of the ACA, may decrease the demand for healthcare services and pharmaceuticals. Additionally, the availability of healthcare services and resources is currently constrained due to the COVID-19 pandemic. If fewer patients are seeking medical care because they do not have insurance coverage or are unable to obtain medical care for their conditions due to resource constraints on the healthcare system, we may experience difficulties in any eventual commercialization of our product 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, including as a result of the COVID-19 pandemic, 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 our product candidates. 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 COVID-19 pandemic, current economic climate and financial market conditions could adversely impact our business.

The global economic conditions created by the conflict between Russia and Ukraine could adversely affect our business, financial condition, stock price and results of operations.

In February 2022, Russia commenced a military invasion of Ukraine, and sustained conflict and disruption in the region is likely. Although the conflict has had little direct impact on our business to date, the uncertainty and ripple effects created by this conflict may have unknown indirect impacts. As a result of the invasion, the U.S. and certain other countries have imposed sanctions on Russia and could impose further sanctions that could damage or disrupt international commerce and the global economy. It is not possible to predict the broader or longer-term consequences of this conflict, or the sanctions imposed to date, which could include further sanctions, embargoes, regional instability, retaliatory cyber-attacks, geopolitical shifts and adverse effects on macroeconomic conditions, security conditions, currency exchange rates and financial markets. The potential effects of the conflict include but are not limited to changes in laws and regulations affecting our business, fluctuations in foreign currency markets, potential supply chain disruptions, and increased market volatility and uncertainty that could have an adverse impact on macroeconomic factors that affect our business and operations.

Our internal computer systems, or those used by our third-party research institution collaborators, CROs or other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our product development programs.

Despite the implementation of security measures, our internal computer systems and those of our current and future CROs and other contractors and consultants may be vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, cybersecurity threats, war, and telecommunication and electrical failures. Although to our knowledge we have not experienced any such material system failure or 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. For example, the loss of clinical trial data from completed, ongoing or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Likewise, we rely on third parties for research and development, the manufacture and supply of drug product and drug substance and to conduct clinical trials and commercialization activities. We depend on these third parties to implement adequate controls and safeguards to protect against and report cyber incidents. If they fail to do so, we may suffer financial and other harm, including to our information, operations, performance, and reputation. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or systems, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development and commercialization of our product candidates could be delayed. We also rely on third-party service providers for aspects of our internal control over financial reporting, and such service providers may experience a material system failure or fail to carry out their obligations in other respects, which may impact our ability to produce accurate and timely financial statements, thus harming our operating results, our ability to operate our business, and our investors' view of us.

Cyber threats, both on premises and in the cloud, are evolving and include, but are not limited to: malicious software, destructive malware, ransomware, attempts to gain unauthorized access to systems or data, disruption to operations, critical systems or denial of service attacks; unauthorized release of confidential, personal or otherwise protected information; corruption of data, networks or systems; harm to individuals; and loss of assets. In addition, we could be impacted by cyber threats or other disruptions or vulnerabilities found in products or services we use that are provided to us by third-parties. The techniques used by criminal elements to attack computer systems are sophisticated, change frequently and may originate from less regulated and remote areas of the world. As a result, we may not be able to address these techniques proactively or implement adequate preventative measures. These events, if not prevented or effectively mitigated, could damage our reputation, require remedial actions and lead to loss of business, regulatory actions, potential liability and other financial losses.

Certain data breaches must also be reported to affected individuals and various government and/or regulatory agencies, and in some cases to the media, under provisions of HIPAA, as amended by HITECH, other U.S. federal and state law, and requirements of non-U.S. jurisdictions, including the EU GDPR and relevant member state law in the EU and other foreign laws, and financial penalties may also apply.

Our insurance policies may not be adequate to compensate us for the potential losses arising from breaches, failures or disruptions of our infrastructure, catastrophic events and disasters or otherwise. In addition, such insurance may not be available to us in the future on economically reasonable terms, or at all. Further, our insurance may not cover all claims made against us and defending a suit, regardless of its merit, could be costly and divert management's attention.

We or the third parties upon whom we depend may be adversely affected by climate change, earthquakes, outbreak of disease, or other natural disasters and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.

Climate change, earthquakes, outbreak of disease, or other natural disasters, including extreme weather events and changing weather patterns such as storms, flooding, droughts, fires and temperature changes, which have become more common, 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, extreme weather risk, power outage, cybersecurity attack 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. For example, we may experience delays in the supply of drug product for our clinical trials as a result of disruptions to the operations of the manufacturing facilities of some of our third-party CMOs due to the global COVID-19 pandemic. Any continued or subsequent measures taken by governmental authorities or business to contain the spread of COVID-19, or the perception that such measures may be required in the future should another outbreak occur, could adversely affect our business, financial condition or results of operations by limiting our CMOs’ ability to manufacture product, forcing closure of facilities that we rely upon or increasing the costs associated with obtaining clinical or commercial supplies of our product candidates. The extent to which the COVID-19 pandemic impacts our results will depend on future developments, which are highly uncertain and cannot be accurately predicted, including new information which may emerge concerning the severity of and duration of COVID-19 pandemic and the actions to contain the pandemic or treat its impact, among others. 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. In addition, cybersecurity liability insurance is difficult to obtain and may not cover any damages we would sustain based on any breach of our computer security protocols or other cybersecurity attack. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which, particularly when taken together with our lack of earthquake insurance, could have a material adverse effect on our business.

Climate change or legal, regulatory or market measures to address climate change may negatively affect our business and results of operations.

Climate change resulting from increased concentrations of carbon dioxide and other greenhouse gases in the atmosphere could present risks to our operations, including an adverse impact on global temperatures, weather patterns and the frequency and severity of extreme weather and natural disasters. Natural disasters and extreme weather conditions, such as a hurricane, tornado, earthquake, wildfire or flooding, may pose physical risks to our facilities and disrupt the operation of our supply chain. The impacts of the changing climate on water resources may result in water scarcity, limiting our ability to access sufficient high-quality water in certain locations, which may increase operational costs. Concern over climate change may also result in new or additional legal or regulatory requirements designed to reduce greenhouse gas emissions and/or mitigate the effects of climate change on the environment. If such laws or regulations are more stringent than current legal or regulatory obligations, we may experience disruption in, or an increase in the costs associated with sourcing, manufacturing and distribution of our product candidates, which may adversely affect our business, results of operations or financial condition. Further, the impacts of climate change have an influence on customer preferences, and failure to provide climate-friendly products could potentially result in loss of market share.

The increasing use of social media platforms presents new risks and challenges.

Social media is increasingly being used to communicate about our research, product candidates, investigational medicines, and the diseases our product candidates and investigational medicines are being developed to treat. 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, resulting in potential regulatory actions against us. 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 our development candidates, investigational medicines and approved products. 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 business operations may subject us to disputes, claims and lawsuits, which may be costly and time-consuming and could materially and adversely impact our financial position and results of operations.

From time to time, we may become involved in disputes, claims and lawsuits relating to our business operations. For example, we may, from time to time, face or initiate claims related to intellectual property matters, employment matters, or commercial disputes. Any dispute, claim or lawsuit may divert management’s attention away from our business, we may incur significant expenses in addressing or defending any dispute, claim or lawsuit, and we may be required to pay damage awards or settlements or become subject to equitable remedies that could adversely affect our operations and financial results. Litigation related to these disputes may be costly and time-consuming and could materially and adversely impact our financial position and results of operations if resolved against us. In addition, the uncertainty associated with litigation could lead to increased volatility in our stock price.

ITEM 1B. UNRESOLVED STAFF COMMENTS

None.

ITEM 2. PROPERTIES

As of December 31, 2022, the following are the material properties that we occupy:

Property Description	Location	Square Footage	Owned or Leased	Initial Lease Term End Date	Lease Extension Options
Office space	Palo Alto, CA	3,900	Leased	2020	Lease will expire in April 2023
Office space and laboratory facility	Raleigh, NC	13,809	Leased	2024	Five-year option to extend
Office space and laboratory facility	Palo Alto, CA	9,789	Leased	2023	Two one-year options to extend
Office space	San Francisco, CA	52,604	Leased	2026	Two-year option to extend
Laboratory facility	Montreal, Québec	20,039	Leased	2032	Five-year option to extend
Office space	San Francisco, CA	10,552	Leased	2026	None

ITEM 3. LEGAL PROCEEDINGS

As of the date of this Annual Report on Form 10-K, we were not party to any material legal proceedings. In the future, we may become party to legal proceedings and claims arising in the ordinary course of business. Although the results of litigation and claims cannot be predicted with certainty, we do not believe we are party to any claim or litigation the outcome of which, if determined adversely to us, would individually or in the aggregate be reasonably expected to have a material adverse impact on our financial position, results of operations or cash flows. Regardless of the outcome, litigation can have an adverse effect on us because of defense and settlement costs, diversion of management resources and other factors.

ITEM 4. MINE SAFETY DISCLOSURES

Not applicable.

PART II

ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES

Market Information

Our common stock began trading on The Nasdaq Global Select Market, or the Nasdaq, under the symbol "BBIO" on June 27, 2019. Prior to that date, there was no public trading market for shares of our common stock.

Holders

As of February 16, 2023, there were 47 stockholders of record of our common stock. As many of our shares of common stock are held by brokers and other institutions on behalf of stockholders, we are unable to estimate the total number of stockholders represented by these record holders.

Dividend Policy

We have never declared or paid any dividends and do not anticipate paying any dividends on our common stock in the foreseeable future. In addition, pursuant to the Loan Agreement, we are not permitted to declare or pay any cash dividends or make cash distributions on any class of our capital stock or any other equity interest, except in limited circumstances.

Securities Authorized for Issuance Under Equity Compensation Plans

Information about our equity compensation plans in Item 12 of Part III of this Annual Report on Form 10-K is incorporated herein by reference.

Stock Performance Graph

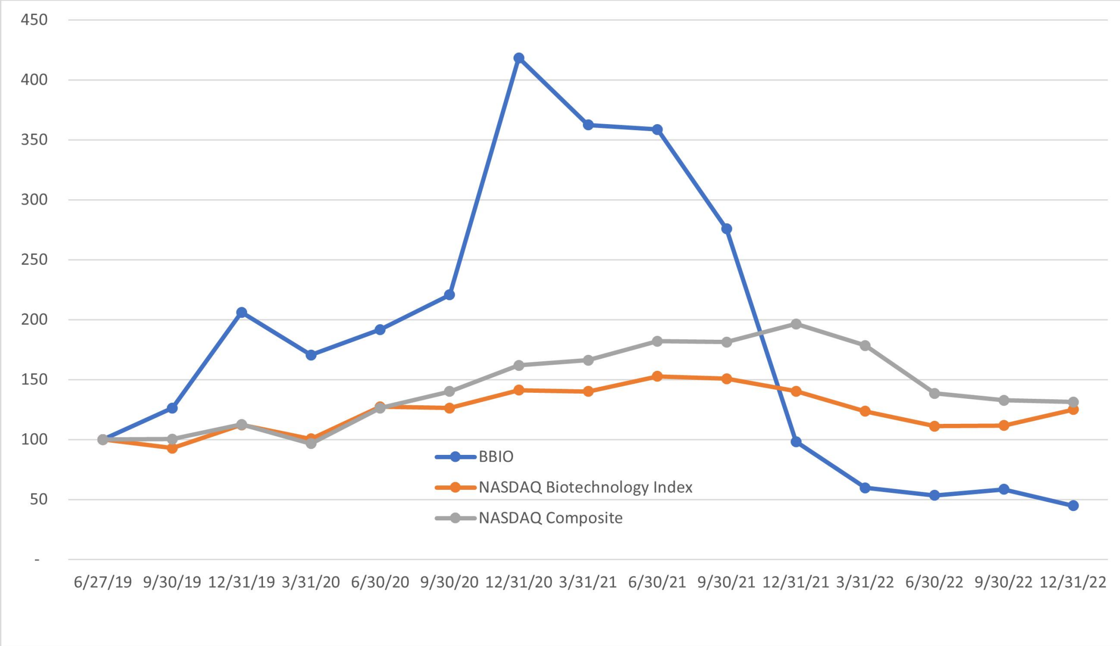
The graph set forth below compares the cumulative total stockholder return on our common stock for the period commencing on June 27, 2019, the date our common stock began trading on the Nasdaq, and ending on December 31, 2022, with the cumulative total return of the Nasdaq Composite Index and the Nasdaq Biotechnology Index over the same period. This graph assumes the investment of $100.00 on June 27, 2019 in each share of our common stock at the initial public offering price of $17.00, the Nasdaq Composite Index, and the Nasdaq Biotechnology Index, and assumes the reinvestment of dividends.

The comparisons shown in the graph below are based upon historical data. We caution that the stock price performance shown in the graph below is not necessarily indicative of, nor is it intended to forecast, the potential future performance of our common stock. Information used in the graph was obtained from sources believed to be reliable including Nasdaq, Bloomberg and Reuters, but we are not responsible for any errors or omissions in such information.

Notwithstanding anything to the contrary set forth in any of our previous or future filings under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, that might incorporate this Annual Report on Form 10-K or future filings made by us under those statutes, this Stock Performance Graph section is not "soliciting material," shall not be deemed filed with the U.S. Securities and Exchange Commission and shall not be deemed incorporated by reference into any of those prior filings or into any future filings made by us under those statutes.

COMPARISON OF CUMULATIVE TOTAL RETURN*

Among BridgeBio Pharma, Inc., the Nasdaq Composite Index and the Nasdaq Biotechnology Index:



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* $100 invested on June 27, 2019 in shares of our common stock or index, including reinvestment of dividends.

Sales of Unregistered Securities

During the year ended December 31, 2022, we did not issue or sell any unregistered securities.

Issuer Purchases of Equity Securities

During the year ended December 31, 2022, we did not repurchase any Company equity securities.

ITEM 6. [Reserved]

ITEM 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

You should read the following discussion and analysis of our financial condition and results of operations together with the financial statements and related notes included elsewhere in this Annual Report on Form 10-K.

This Annual Report on Form 10-K contains "forward-looking statements" within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. In some cases, you can identify these statements by forward-looking words such as "may," "will," "expect," "believe," "anticipate," "intend," "could," "should," "estimate," or "continue," and similar expressions or variations. Such forward-looking statements are subject to risks, uncertainties and other factors that could cause actual results and the timing of certain events to differ materially from future results expressed or implied by such forward-looking statements. Factors that could cause or contribute to such differences include, but are not limited to, those identified below, and those discussed in the section titled "Risk Factors" included in this Annual Report on Form 10-K. The forward-looking statements in this Annual Report on Form 10-K represent our views as of the date of this Annual Report on Form 10-K. Except as may be required by law, we assume no obligation to update these forward-looking statements or the reasons that results could differ from these forward-looking statements. You should, therefore, not rely on these forward-looking statements as representing our views as of any date subsequent to the date of this Annual Report on Form 10-K.

Overview

BridgeBio Pharma, Inc. ("we" or the "Company") is a commercial-stage biopharmaceutical company founded to discover, create, test and deliver transformative medicines to treat patients who suffer from genetic diseases and cancers with clear genetic drivers. BridgeBio's pipeline of development programs ranges from early science to advanced clinical trials. BridgeBio was founded in 2015 and its team of experienced drug discoverers, developers and innovators are committed to applying advances in genetic medicine to help patients as quickly as possible. Since inception, BridgeBio has created 15 Investigational New Drug applications, or INDs, and had two products approved by the U.S. Food and Drug Administration. We work across over 20 disease states at various stages of development. Several of our programs target indications that we believe present the potential for our product candidates, if approved, to target portions of market opportunities of at least $1.0 billion in annual sales.

We focus on genetic diseases because they exist at the intersection of high unmet patient need and tractable biology. Our approach is to translate research pioneered at academic laboratories and leading medical institutions into products that we hope will ultimately reach patients. We are able to realize this opportunity through a confluence of scientific advances: (i) identification of the genetic underpinnings of disease as more cost-efficient genome and exome sequencing becomes available; (ii) progress in molecular biology; and (iii) the development and maturation of longitudinal data and retrospective studies that enable the linkage of genes to diseases. We believe that this early-stage innovation represents one of the greatest practical sources for new drug creation.

Since our inception in 2015, we have focused substantially all of our efforts and financial resources on acquiring and developing product and technology rights, building our intellectual property portfolio and conducting research and development activities for our product candidates within our wholly-owned subsidiaries and controlled entities, including partially-owned subsidiaries and subsidiaries we consolidate based on our deemed majority control of such entities as determined using either the variable interest entity, or VIE model, or the voting interest entity, or VOE model. To support these activities, we and our wholly-owned subsidiary, BridgeBio Services, Inc., (i) identify and secure new programs, (ii) set up new wholly-owned subsidiaries or controlled entities, (iii) recruit key management team members, (iv) raise and allocate capital across the portfolio and (v) provide certain shared services, including accounting, legal, information technology and human resources, as well as workspaces. We have not generated any significant revenue from product sales. We do not anticipate generating any revenues from our product sales for the near term as the selling activities for our two FDA-approved products have been transferred or transitioned to our respective partners. To date, we have funded our operations with proceeds from the sale of our equity securities, issuance of convertible notes, debt borrowings, sale of certain assets and, to a lesser extent, revenue from licensing arrangements.

Since our inception, we have incurred significant operating losses. For the years ended December 31, 2022, 2021 and 2020, we incurred net losses of $484.7 million, $586.5 million and $505.5 million, respectively. Our ability to generate product revenue sufficient to achieve profitability will depend heavily on the successful development and eventual commercialization of our product candidates at our wholly-owned subsidiaries and controlled entities. We expect to continue to incur operating and net losses for at least the next several years.

Due to the inherently unpredictable nature of preclinical and clinical development, and given our novel therapeutic approaches and the stage of development of our product candidates, we cannot determine and are unable to estimate with certainty the timelines we will require and the costs we will incur for the development of our product candidates. Clinical and preclinical development timelines and costs, and the potential of development success, can differ materially from expectations due to a variety of factors. For example, in light of the continuing impact of COVID-19 and the focus of healthcare providers and hospitals on the virus and its variants, we have experienced delays in or temporary suspensions of the enrollment of patients in our subsidiaries' ongoing clinical trials. We additionally may experience delays in certain ongoing activities, including commencement of planned clinical trials, non-clinical experiments and IND-enabling good laboratory practice toxicology studies. The duration of delays and their overall impact on our business are currently unknown, and we are continuing to monitor the situation. The continued spread of COVID-19 has resulted in significant governmental measures worldwide. These measures may result in business, supply, and drug product manufacturing disruptions and in reduced operations, any of which could materially affect our business, financial condition and results of operations. Accordingly, we may take further precautionary and preemptive actions as may be required by federal, state or local authorities or that we determine are in the best interests of public health and safety and that of our patient community, employees, partners, suppliers and stockholders. We cannot predict the effects that such actions, the duration of the COVID-19 pandemic, or its continuing impact may have on our business or strategy, including the effects on our ongoing and planned clinical development activities and prospects, or on our financial and operating results.

In January 2022, we committed to a restructuring initiative designed to drive operational changes in our business processes, efficiencies and cost savings to advance our corporate strategy and development programs. The restructuring initiative included, among other components, consolidation and rationalization of our facilities, reprioritization of development programs and the reduction in our workforce. During the fiscal year ended December 31, 2022, our restructuring, impairment and related charges amounted to $43.8 million which consisted primarily of winding down costs, exit and other related costs, impairments and write-offs of long-lived assets, and severance and employee-related costs. We are continuing to evaluate our restructuring initiatives for the fiscal year ending 2023 and we estimate to incur total charges in the range of approximately $6.0 million to $9.0 million. Our estimate of the range of costs is subject to certain assumptions and actual results may differ from those estimates or assumptions. We may also incur additional costs that are not currently foreseeable as we continue to evaluate our restructuring alternatives to drive operational changes in our business processes, efficiencies, and cost savings.

On August 23, 2022, we received written notice from Helsinn Group, or Helsinn, of its intent to terminate the Amended and Restated License and Collaboration Agreement ("Amended QED-Helsinn License and Collaboration Agreement") for convenience, pursuant to its terms, citing commercial considerations. Effective December 21, 2022, our subsidiary, QED Therapeutics, Inc, or QED, and Helsinn, or the Helsinn Parties, entered into a Mutual Termination Agreement or MTA which terminates the Amended QED-Helsinn License and Collaboration Agreement and all rights and obligations thereunder. The Helsinn Parties agree to perform certain close-out services to enable QED to pursue the development, manufacture and commercialization of infigratinib as a potential treatment of non-oncology indications, such as in achondroplasia worldwide, excluding China, Hong Kong, and Macau. As a result of the termination, QED will no longer be entitled to any future regulatory or sales-based milestone payments. QED will be subject to royalties on net sales of TRUSELTIQ until Helsinn no longer sells the licensed product by March 31, 2023. The Helsinn Parties have delivered notice to the FDA notifying them that the distribution of TRUSELTIQ is permanently discontinued and that all clinical investigations under the associated IND are discontinued. We expect that the licensed product will be sold through the first quarter of 2023. The Helsinn Parties have developed a Close-Out Plan, as defined within the MTA. Activities within the Close-Out Plan are to be shared equally subsequent to the first $11.0 million of costs, which are the responsibility of QED. The activities within the Close-Out Plan are expected to be completed during 2023.

Basis of Presentation and Consolidation

Since our inception, we have created wholly-owned subsidiaries or made investments in certain controlled entities, including partially-owned subsidiaries for which we have majority voting interest under the VOE model or for which we are the primary beneficiary under the VIE model, which we refer to collectively as our consolidated entities. Ownership interests in consolidated entities that are held by entities other than us are reported as redeemable convertible noncontrolling interests and noncontrolling interests in our consolidated balance sheets. Losses attributed to redeemable convertible noncontrolling interests and noncontrolling interests are reported separately in our consolidated statements of operations.

Results of Operations

Comparison of the years ended December 31, 2022 and 2021

We have included our financial results for 2022 compared to 2021. Additional information required by Item 7 for the year ended December 31, 2020 can be found in Item 7 in our Annual Report on Form 10-K for the year ended December 31, 2021, filed with the U.S. Securities and Exchange Commission, or the SEC, on February 25, 2022 and is incorporated herein by reference.

The following table summarizes the results of our operations for the periods indicated:

	Year Ended December 31,		
	2022	2021	Change
	(in thousands)		
License and services revenue	$ 76,094	$ 65,923	$ 10,171
Product sales	1,554	3,793	(2,239)
Cost of license revenue and products sold	3,434	3,114	320
Research and development	399,462	451,024	(51,562)
Selling, general and administrative	143,189	192,210	(49,021)
Restructuring, impairment and related charges	43,765	—	43,765
Loss from operations	(512,202)	(576,632)	64,430
Gain from sale of priority review voucher, net	107,946	—	107,946
Net loss	(484,652)	(586,454)	101,802
Net loss attributable to common stockholders of BridgeBio	(481,183)	(562,539)	81,356
Cash, cash equivalents and marketable securities	428,269	787,515	(359,246)
Restricted cash	37,930	177	37,753
Investment in equity securities	43,653	49,148	(5,495)

The results of operations for the years ended December 31, 2022 and 2021 are not necessarily indicative of the results to be expected for the year ending December 31, 2023 or for any other future annual or interim period.

Cash, Cash Equivalents, Marketable Securities, Restricted Cash and Investment in Equity Securities

As of December 31, 2022, we had cash, cash equivalents and marketable securities of $428.3 million, restricted cash of $37.9 million and investment in equity securities of $43.7 million. Restricted cash primarily represents funds in a controlled account that was established in connection with the Second Amendment of the Company’s Loan and Security Agreement that is described in Note 10. The use of such non-interest-bearing cash is restricted per the terms of the underlying amended loan agreement and is to be used solely for certain research and development expenses directly attributable to the performance of obligations associated with the Navire-BMS License Agreement, which is further described in Note 11. We consider our investment in equity securities as a source of our liquidity as we may liquidate these shares to fund current operations, should the need arise.

In March 2022, we received an upfront payment of $10.0 million upon the closing of the asset purchase agreement ("APA") between our subsidiary, Origin Biosciences, Inc, (Origin"), and Sentynl Therapeutics, Inc. ("Sentynl") or the Origin-Sentynl APA.

In June 2022, we received $90.0 million in upfront payment from the License and Collaboration Agreement that our subsidiary, Navire Pharma, Inc., (“Navire”) entered into with Bristol-Myers Squibb Company, (“BMS’), referred to as the Navire-BMS License Agreement. The receipt of the upfront payment from BMS triggered certain mandatory prepayment provisions of our Amended Loan Agreement, which is further described in the succeeding sections, and, as a result, we paid $20.5 million to our lenders and segregated $37.8 million in a controlled account for the year ended December 31, 2022.

In June 2022, we received gross proceeds of $110.0 million from the sale of our Priority Review Voucher (“PRV”) and recognized a net gain of $107.9 million, net of transaction costs for the year ended December 31, 2022.

In November 2022, we received net proceeds of $4.9 million from the issuance of our common stock under the “at-the-market” (“ATM”) offering as part of our filed 2020 shelf registration.

Revenue

	Year Ended December 31, 2022	2021	Change
		(in thousands)	
Revenue:			
License and services revenue	$ 76,094	$ 65,923	$ 10,171
Product sales	1,554	3,793	(2,239)
Total revenue	$ 77,648	$ 69,716	$ 7,932

License and services revenue consists mainly of the recognition of upfront license, milestone payments and services revenue in connection with our license and collaboration agreements. The level of license and services revenue to be recognized depends in part upon the estimated recognition period of the upfront payments allocated to continuing performance obligations, the achievement of milestones and other contingent events, the level of effort incurred for research and development contracted services, and entering into new collaboration agreements, if any.

License and services revenue for the year ended December 31, 2022 was $76.1 million, of which $74.7 million relates to the recognition of upfront license and services revenue in connection with the License and Collaboration Agreement entered into in May 2022 between Navire and BMS, or the Navire-BMS License Agreement. The remaining amount mainly relates to the recognition of revenue related to royalties received for the sale of commercial product that was transferred to our collaboration partners and product supplied to our collaboration partners.

License and services revenue for the year ended December 31, 2021 was $65.9 million, of which:

- $56.0 million primarily relates to the recognition of upfront, launch and regulatory-related milestone payments in connection with the License and Collaboration Agreement entered into in March 2021 between our subsidiary, QED and Helsinn, or the QED-Helsinn License and Collaboration Agreement, and
- $8.5 million relates to the recognition of regulatory milestone achievement under the License Agreement between Navire, and LianBio.

Transactions with LianBio were considered related party transactions up until its initial public offering, or IPO, in November 2021, when our right to appoint or remove one director to the board of directors of LianBio was terminated (see Note 7 to our consolidated financial statements). LianBio is no longer considered a related party after its IPO.

Operating Costs and Expenses

Research and Development Expenses

	Year Ended December 31,		
	2022	2021	Change
	(in thousands)		
Research and development	$ 399,462	$ 451,024	$ (51,562)

Research and development expenses decreased by $51.6 million in 2022 compared to 2021 primarily due to a decrease in external costs and stock-based compensation costs as a result of the reprioritization of our development programs in line with our restructuring initiative. Stock-based compensation recorded in research and development expense in 2022 was $38.0 million as compared to $56.2 million in 2021. The decrease was mainly driven by a higher number of performance-based milestone compensation arrangements for regulatory and development milestones achieved and determined to be probable as of December 31, 2021 compared to those that were achieved and determined to be probable as of December 31, 2022. The decrease in external costs was partially offset by the lower reduction of research and development expenses in fiscal year 2022 compared to fiscal year 2021 as a result of QED-Helsinn License and Collaboration Agreement discussed below.

Pursuant to the QED-Helsinn License and Collaboration Agreement, Helsinn shared 60% of our research and development costs for infigratinib for certain indications as stipulated under the agreement. Upon the effective date of the Amended QED-Helsinn License and Collaboration Agreement, Helsinn is solely responsible for development costs for infigratinib for certain indications and our incurred costs during the transitional period are fully reimbursable. As discussed in the Overview section in *Item 2. Management's Discussion and Analysis of Financial Condition and Results of Operations*, Helsinn notified us on August 23, 2022 of their intent to terminate the Amended QED-Helsinn License and Collaboration Agreement. Effective December 21, 2022, the Helsinn Parties entered into a MTA which terminates the Amended QED-Helsinn License and Collaboration Agreement and all rights and obligations thereunder. The Helsinn Parties agree to perform certain close-out services to enable QED to pursue the development, manufacture and commercialization of infigratinib as a potential treatment of non-oncology indications, such as in achondroplasia worldwide, excluding China, Hong Kong, and Macau. All close-out costs are presented as part of "Restructuring, impairment and related charges" on our consolidated statements of operations.

- For the year ended December 31, 2022, Helsinn's share of the research and development costs under the QED-Helsinn License and Collaboration Agreement amounted to $2.9 million which was reflected as a reduction of research and development expenses. The comparative amount was $38.4 million for the year ended December 31, 2021, which was reflected as a reduction of research and development expenses.
- In accordance with the Amended QED-Helsinn License and Collaboration Agreement, which became effective on March 1, 2022, we have recognized $18.6 million as a reduction of research and development expenses for the year ended December 31, 2022, which represents 100% reimbursement of research and development costs incurred during the transitional period.

Refer to Note 11 to our consolidated financial statements for more information on the QED-Helsinn License and Collaboration Agreement, the Amended QED-Helsinn License and Collaboration Agreement and the termination of the QED-Helsinn License and Collaboration Agreement.

Research and development costs consist primarily of external costs, such as fees paid to consultants, contractors, contract manufacturing organizations, or CMOs, and contract research organizations, or CROs, in connection with our preclinical and clinical development activities and are tracked on a program-by-program basis. License fees and other costs incurred after a product candidate has been designated and that are directly related to the product candidate are included in the specific program expense. License fees and other costs incurred prior to designating a product candidate are included in other development programs as shown in the table below.

The following table summarizes our research and development expenses by program incurred for the following periods:

	Year Ended December 31,	
	2022	2021
	(in thousands)	
Acoramidis (Previously known as AG10)	$ 91,901	$ 107,806
Low-dose infigratinib for achondroplasia	32,387	40,650
BBP-418 for Limb-Girdle Muscular Dystrophy type 2I, or LGMD2I	22,372	15,202
Encaleret	27,485	15,739
BBP-631	34,009	46,035
KRAS inhibitor portfolio	33,216	15,554
Other development programs	90,492	147,303
Other research programs	67,600	62,735
Total	$ 399,462	$ 451,024

Selling, General and Administrative Expenses

	Year Ended December 31,		
	2022	2021	Change
	(in thousands)		
Selling, general and administrative	$ 143,189	$ 192,210	$ (49,021)

Selling, general and administrative expenses decreased by $49.0 million in 2022 compared to 2021, mainly due to the streamlining of costs as a result of our restructuring initiative. Stock-based compensation recorded in selling, general and administrative expense in 2022 was $54.7 million as compared to $49.4 million in the prior year. The increase is mainly driven by higher grants awarded in the first quarter of 2022 and towards the end of 2021.

Under the QED-Helsinn License and Collaboration Agreement, the Helsinn Parties co-commercialized TRUSELTIQ in the United States and shared profits and losses on a 50:50 basis. Upon the effective date of the Amended QED-Helsinn License and Collaboration Agreement, Helsinn is solely responsible for the commercialization of TRUSELTIQ and our incurred costs during the transitional period are fully reimbursable. As discussed in the Overview section in *Item 2. Management's Discussion and Analysis of Financial Condition and Results of Operations,* Helsinn notified us on August 23, 2022 of their intent to terminate the Amended QED-Helsinn License and Collaboration Agreement. Effective December 21, 2022, the Helsinn Parties entered into a MTA which terminates the Amended QED-Helsinn License and Collaboration Agreement and all rights and obligations thereunder. The Helsinn Parties agree to perform certain close-out services to enable QED to pursue the development, manufacture and commercialization of infigratinib as a potential treatment of non-oncology indications, such as in achondroplasia worldwide, excluding China, Hong Kong, and Macau. All close-out costs are presented as part of "Restructuring, impairment and related charges" on our consolidated statements of operations.

We accounted for Helsinn's share of the commercialization loss of $1.3 million under the QED-Helsinn License and Collaboration Agreement as a reduction of selling, general and administrative for the year ended December 31, 2022. The comparative amount was $8.9 million for the year ended December 31, 2021.

Restructuring, Impairment and Related Charges

	Year Ended December 31,		
	2022	2021	Change
	(in thousands)		
Restructuring, impairment and related charges	$ 43,765	$ —	$ 43,765

As discussed in Note 17 to our consolidated financial statements, in January 2022, we committed to a restructuring initiative designed to drive operational changes in our business processes, efficiencies and cost savings to advance our corporate strategy and development programs. The restructuring initiative included, among other components, consolidation and rationalization of our facilities, reprioritization of development programs and the reduction in our workforce. The charges incurred during the year ended December 31, 2022, consisted primarily of winding down costs, exit and other related costs, impairments and write-offs of long-lived assets, and severance and employee-related costs. We are continuing to evaluate our restructuring initiatives for fiscal year 2023 and we estimate to incur total charges in the range of approximately $6.0 million to $9.0 million. Our estimate of the range of costs is subject to certain assumptions and actual results may differ from those estimates or assumptions. We may also incur additional costs that are not currently foreseeable as we continue to evaluate our restructuring alternatives to drive operational changes in business processes, efficiencies and cost savings.

Other Income (Expense), Net

Interest Income

	Year Ended December 31,		
	2022	2021	Change
		(in thousands)	
Interest income	$ 7,542	$ 1,133	$ 6,409

Interest income consists of interest income earned on our cash equivalents and marketable securities. The increase in interest income is due to higher interest rates and average balances of our interest-bearing cash accounts.

Interest Expense

	Year Ended December 31,		
	2022	2021	Change
		(in thousands)	
Interest expense	$ (80,438)	$ (46,778)	$ (33,660)

Interest expense in 2022 consists primarily of interest expense incurred under our 2029 Notes issued in January 2021, our 2027 Notes issued in March 2020, and our term loan with various lenders under the Loan Agreement dated November 17, 2021.

Interest expense in 2021 consists primarily of interest expense incurred under our 2029 Notes, our 2027 Notes, our now fully-paid term loan with Hercules Capital, Inc., or Hercules, pursuant to our Loan and Security Agreement, dated June 19, 2018, as amended from time to time, and our now fully-paid term loan with Silicon Valley Bank, or SVB, and Hercules pursuant to the Loan and Security Agreement, dated November 13, 2019, or the SVB and Hercules Loan Agreement.

The increase of $33.7 million in 2022 compared to 2021 was primarily attributed to an increase in principal amounts of our debt with the term loan being drawn in November 2021 and we exercised our option to pay the interest in kind in 2022.

Gain From Sale of Priority Review Voucher, net

	Year Ended December 31,		
	2022	2021	Change
		(in thousands)	
Gain from sale of priority review voucher, net	$ 107,946	$ —	$ 107,946

In May 2022, we announced that we entered into a definitive agreement to sell our PRV for $110.0 million. We received the PRV in February 2021 under a U.S. Food and Drug Administration program intended to encourage the development of treatments for rare pediatric diseases. We were awarded the PRV when our subsidiary Origin received approval of NULIBRY. The PRV sale was subject to customary closing conditions and was completed in June 2022 following the expiration of applicable U.S. antitrust clearance requirements. We received the gross proceeds of $110.0 million during the year ended December 31, 2022 and recognized a net gain of $107.9 million, net of transaction costs for the year ended December 31, 2022.

Other Income (Expense), net

	Year Ended December 31,		
	2022	2021	Change
		(in thousands)	
Other income (expense), net	$ (7,500)	$ 35,823	$ (43,323)

Other income (expense), net in 2022 consists mainly of net realized and unrealized losses from changes in the fair value of our equity security investment of $8.2 million, loss from disposal of Origin's assets of $6.3 million, and the expense associated with the Origin regulatory milestone of $3.5 million, partially offset by a gain from the recognition of a receivable of $12.5 million from Helsinn under the Amended QED-Helsinn License and Collaboration Agreement.

Other income (expense), net in 2021 consists mainly of the unrealized gain on conversion of our equity method investment in LianBio to investment in equity security of $68.5 million upon LianBio's IPO in November 2021, partially offset by unrealized losses from changes in fair value of such equity security investment through December 31, 2021 of $37.7 million (see Note 7 to our consolidated financial statements) and loss on early extinguishment of our debt of $3.3 million. Other income (expense), net during the year also includes changes in fair value of the LEO Call Option liability. In March 2021, LEO elected to terminate the LEO Call Option, which resulted in derecognition of the LEO Call Option liability of $5.6 million.

Income Taxes

We are subject to U.S. federal, state and foreign income taxes as a corporation. For U.S. federal income tax purposes, we are required to file a consolidated U.S. federal income tax return for the consolidated entities that meet the requirements as prescribed by the consolidated regulations. Those entities that do not meet the threshold to be included in the consolidated filing continue to file separate U.S. federal income tax returns. To the extent we incur operating losses in the periods in which we are treated as a corporation for tax purposes, net operating loss carryforwards may generally be used by us to offset cash taxes on future taxable income, subject to applicable tax laws.

Beginning in 2022, the 2017 Tax Cuts and Jobs Act amended Section 174 to eliminate current-year deductibility of research and experimentation (R&E) expenditures and software development costs (collectively, R&E expenditures) and instead require taxpayers to charge their R&E expenditures to a capital account amortized over five years (15 years for expenditures attributable to R&E activity performed outside the United States). We realized a deferred tax asset for capitalized R&E expenditures for the year ended December 31, 2022 which is fully offset with a valuation allowance.

As of December 31, 2022, we had net operating losses of approximately $1.4 billion and $255.4 million for federal and state income tax purposes, respectively, available to reduce future taxable income, if any. The federal net operating losses generated prior to 2018 in the amount of $37.5 million will begin to expire in 2035 and losses generated after 2018 in the amount of $1.4 billion will carry over indefinitely and would be subject to an 80% taxable income limitation in the year utilized. State net operating losses will generally begin to expire in 2038. As of December 31, 2022, we had federal research and development and orphan drug credit carryforwards of $92.7 million, which will expire beginning in 2036 if not utilized. As of December 31, 2022, we had state research and development credit carryforwards of $17.2 million. The state research and development tax credits will expire at various dates while the California research and development tax credits will carry over indefinitely.

A valuation allowance is provided for deferred tax assets where the recoverability of the assets is uncertain. The determination to provide a valuation allowance is dependent upon the assessment of whether it is more likely than not that sufficient future taxable income will be generated to utilize the deferred tax assets. Based on the weight of the available evidence, which includes our consolidated entities' historical operating losses and forecast of future losses, we have provided a valuation allowance against the US Federal and state deferred tax assets resulting from the tax loss and credits carried forward. As a result of the issuance of our 2027 Notes in 2020, it was determined that our existing deferred tax assets do not fully offset the deferred tax liabilities when reviewing the reversals of temporary differences. This resulted in a deferred tax liability of $1.1 million that was recognized for the year ended December 31, 2020. We have derecognized the deferred tax liability on January 1, 2021 upon early adoption of ASU 2020-06, with no impact on the provision for income tax. The valuation allowance increased by $110.0 million and $199.5 million for the years ended December 31, 2022 and 2021, respectively.

Utilization of the net operating loss and credit carryforwards may be subject to a substantial annual limitation due to an ownership change limitation as provided by section 382 of the Internal Revenue Code of 1986, as amended, or the Code, and similar state provisions. The annual limitation may result in the expiration of net operating losses and credits before utilization. In the event that we have a change of ownership, utilization of the net operating loss and tax credit carryforwards may be restricted.

Net Loss Attributable to Redeemable Convertible Noncontrolling Interests and Noncontrolling Interests

Net loss attributable to redeemable convertible noncontrolling interests and noncontrolling interests in our consolidated statements of operations consists of the portion of the net loss of those consolidated entities that is not allocated to us. Changes in the amount of net loss attributable to noncontrolling interests are directly impacted by changes in the net loss of our consolidated entities and are the result of ownership percentage changes. Refer to Note 6 to our consolidated financial statements.

Net loss attributable to redeemable convertible noncontrolling interests and noncontrolling interests was $3.5 million in 2022, compared to $23.9 million in 2021.

Liquidity and Capital Resources

We have historically financed our operations primarily through the sale of our equity securities, issuance of convertible notes, debt borrowings, revenue from certain licensing arrangements and sale of certain assets. As of December 31, 2022, we had cash, cash equivalents and marketable securities of $428.3 million, restricted cash of $37.9 million and investment in equity securities of $43.7 million. We consider our investment in equity securities as a source of our liquidity as we may liquidate these shares to fund current operations, should the need arise. Restricted cash related to the Navire-BMS License Agreement under the Loan agreement was $37.8 million, which is presented as part of "Restricted cash" on the consolidated balance sheets. The funds that were held by our wholly-owned subsidiaries and controlled entities are available for specific entity usage, except in limited circumstances. As of December 31, 2022, our outstanding debt was $1.7 billion, net of debt issuance costs and accretion.

Since our inception, we have incurred significant operating losses. For the years ended December 31, 2022, 2021 and 2020, we incurred net losses of $484.7 million, $586.5 million and $505.5 million, respectively. We incurred net cash outflow from operations of $419.5 million, $497.9 million, and $399.7 million for the same periods, respectively. We had an accumulated deficit as of December 31, 2022 of $1.9 billion. While we have undertaken a restructuring initiative to drive operational change in business processes, efficiencies and cost savings, we expect to continue to incur operating and net losses over the next several years as we continue to fund our drug development and discovery efforts, as well as costs related to commercial launch readiness for our late-stage programs. In particular, to the extent we advance our programs into and through later-stage clinical trials without a partner, we will incur substantial expenses. Our current business plan is also subject to significant uncertainties and risks as a result of, among other factors, our ability to generate product sales sufficient to achieve profitability, which will depend heavily on the successful development and eventual commercialization of our product candidates at our consolidated entities as well as our ability to partner in the development of certain clinical programs.

Our short-term and long-term liquidity requirements include contractual payments related to our 2029 Notes, 2027 Notes and term loan (see Note 10 to our consolidated financial statements), as well as obligations under our real estate leases (see Note 14 to our consolidated financial statements) and the remaining liabilities under our restructuring initiative (see Note 17 to our consolidated financial statements).

We also have performance-based milestone compensation arrangements with certain employees and consultants, whose vesting is contingent upon meeting various regulatory and development milestones, with fixed monetary amounts known at inception that can be settled in the form of cash or equity at our sole election, upon achievement of each contingent milestone (see Note 9 to our consolidated financial statements).

Additionally, we have certain contingent payment obligations under various license and collaboration agreements in which we are required to make milestone payments upon successful completion and achievement of certain intellectual property, clinical, regulatory and sales milestones. We also enter into agreements in the normal course of business with CROs and other vendors for clinical trials and with vendors for preclinical studies and other services and products for operating purposes, which are generally cancelable upon written notice with potential termination charges.

We expect our cash and cash equivalents, marketable securities, restricted cash, and investment in equity securities will fund our operations for at least the next 12 months based on current operating plans and financial forecasts. If our current operating plans or financial forecasts change, including as a result of general market and economic conditions, inflationary pressures, supply chain issues and the effects of the ongoing COVID-19 pandemic on our research and development activities, we may require additional funding sooner in the form of public or private equity offerings, debt financings or additional collaborations and licensing arrangements. However, future financing may not be available in amounts or on terms acceptable to us, if at all.

In addition, we are closely monitoring ongoing developments in connection with the continuing COVID-19 pandemic and inflationary pressures, which may negatively impact our financial and operating results. We will continue to assess our operating costs and expenses and our cash and cash equivalents and, if circumstances warrant, we will make appropriate adjustments to our operating plan.

Sources of Liquidity

Initial public offerings and at-the-market share issuances

On July 7, 2020, we filed a shelf registration statement on Form S-3ASR, or the 2020 Shelf, with the SEC in relation to the registration of common stock, preferred stock, debt securities, warrants and units or any combination thereof. We also simultaneously entered into an Open Market Sale Agreement, or the 2020 Sales Agreement, with Jefferies LLC and SVB Leerink LLC, or collectively, the Sales Agents, to provide for the offering, issuance and sale by us of up to an aggregate of $350.0 million of our common stock from time to time in “at-the-market” offerings under the 2020 Shelf and subject to the limitations thereof. We will pay to the applicable Sales Agents cash commissions of up to 3.0% of the gross proceeds of sales of common stock under the 2020 Sales Agreement. During the year ended December 31, 2022, the Company sold 455,800 shares through this offering at an average price of $10.90 per share, resulting in net proceeds of $4.9 million. As of December 31, 2022, the Company is still eligible to sell up to $345.0 million of our common stock pursuant to the 2020 Sales Agreement under the 2020 Shelf.

Debt

As of December 31, 2022, we have borrowings under the 2029 Notes, the 2027 Notes and the Loan Agreement, which are discussed below. As of December 31, 2021, our debt consisted of borrowings under the 2029 Notes, 2027 Notes, as well as term loans under the Amended Hercules Loan and Security Agreement and the Silicon Valley Bank and Hercules Loan and Security Agreement, both of which were prepaid in full during 2021.

2029 Notes

In January 2021, we issued an aggregate principal amount of $747.5 million of our 2029 Notes, pursuant to an Indenture dated January 28, 2021, or the 2029 Notes Indenture, between us and U.S. Bank National Association, as trustee, or the 2029 Notes Trustee, in a private offering to qualified institutional buyers, or the 2021 Note Offering, pursuant to Rule 144A under the Securities Act.

The 2029 Notes accrue interest payable semiannually in arrears on February 1 and August 1 of each year, beginning on August 1, 2021, at a rate of 2.25% per year. The 2029 Notes will mature on February 1, 2029, unless earlier converted, redeemed or repurchased. The 2029 Notes are convertible into cash, shares of our common stock or a combination of cash and shares of our common stock, at our election.

We received net proceeds from the 2021 Note Offering of approximately $731.4 million, after deducting the 2029 Notes Initial Purchasers’ discount. There were no direct offering expenses borne by us for the 2029 Notes. We used approximately $61.3 million of the net proceeds from the 2021 Note Offering to pay for the cost of the 2021 Capped Call Transactions and approximately $50.0 million to pay for the repurchase of shares of our common stock.

A holder of 2029 Notes may convert all or any portion of its 2029 Notes at its option at any time prior to the close of business on the business day immediately preceding November 1, 2028 only under certain circumstances.

On or after November 1, 2028 until the close of business on the second scheduled trading day immediately preceding the maturity date, a holder may convert all or any portion of its 2029 Notes at any time.

We may not redeem the 2029 Notes prior to February 6, 2026. We may redeem for cash all or any portion of the 2029 Notes, at our option, on a redemption date occurring on or after February 6, 2026, and on or before the 41st scheduled trading day immediately before the maturity date, under certain circumstances. No sinking fund is provided for the 2029 Notes. If we undergo a fundamental change (as defined in the 2029 Notes Indenture), holders may require us to repurchase for cash all or any portion of their 2029 Notes at a fundamental change repurchase price equal to 100% of the principal amount of the 2029 Notes to be repurchased, plus any accrued and unpaid interest to, but excluding, the fundamental change repurchase date. The 2029 Notes Indenture contains customary terms and covenants, including that upon certain events of default occurring and continuing, either the 2029 Notes Trustee or the holders of not less than 25% in aggregate principal amount of the 2029 Notes then outstanding may declare the entire principal amount of all the Notes plus accrued special interest, if any, to be immediately due and payable. The 2029 Notes are our general unsecured obligations and rank senior in right of payment to all of our indebtedness that is expressly subordinated in right of payment to the 2029 Notes; equal in right of payment with all of our liabilities that are not so subordinated, including our 2027 Notes; effectively junior to any of our secured indebtedness to the extent of the value of the assets securing such indebtedness; and structurally junior to all indebtedness and other liabilities (including trade payables) of our subsidiaries.

Refer to Note 10 in our consolidated financial statements for other details, including our future minimum payments under the 2029 Notes.

2027 Notes

In March 2020, we issued an aggregate principal amount of $550.0 million of our 2027 Notes, pursuant to an Indenture dated March 9, 2020, or the Indenture, between BridgeBio and U.S. Bank National Association, as trustee, or the Trustee, in a private offering to qualified institutional buyers, or the 2020 Note Offering, pursuant to Rule 144A under the Securities Act.

The 2027 Notes are senior, unsecured obligations of BridgeBio and accrue interest payable semiannually in arrears on March 15 and September 15 of each year, beginning on September 15, 2020, at a rate of 2.50% per year. The 2027 Notes will mature on March 15, 2027, unless earlier converted or repurchased. Upon conversion, the 2027 Notes are convertible into cash, shares of our common stock or a combination of cash and shares of our common stock, at our election.

We received net proceeds from the 2020 Note Offering of approximately $537.0 million, after deducting the Initial Purchasers' discount and offering expenses. We used approximately $49.3 million of the net proceeds from the 2020 Note Offering to pay for the cost of the Capped Call Transactions, and approximately $75.0 million to pay for the repurchases of shares of our common stock in connection with the 2020 Note Offering.

A holder of 2027 Notes may convert all or any portion of its 2027 Notes at its option at any time prior to the close of business on the business day immediately preceding December 15, 2026 only under certain circumstances.

On or after December 15, 2026 until the close of business on the second scheduled trading day immediately preceding the maturity date, a holder may convert all or any portion of its 2027 Notes at any time.

We may not redeem the 2027 Notes prior to the maturity date, and no sinking fund is provided for the 2027 Notes. If we undergo a fundamental change (as defined in the Indenture), holders may require us to repurchase for cash all or any portion of their 2027 Notes at a fundamental change repurchase price equal to 100% of the principal amount of the 2027 Notes to be repurchased, plus any accrued and unpaid interest to, but excluding, the fundamental change repurchase date. The Indenture contains customary terms and covenants, including that upon certain events of default occurring and continuing, either the Trustee or the holders of not less than 25% in aggregate principal amount of the 2027 Notes then outstanding may declare the entire principal amount of all the Notes plus accrued special interest, if any, to be immediately due and payable. The 2027 Notes are our general unsecured obligations and rank senior in right of payment to all of our indebtedness that is expressly subordinated in right of payment to the 2027 Notes; equal in right of payment with all of our liabilities that are not so subordinated; effectively junior to any of our secured indebtedness to the extent of the value of the assets securing such indebtedness; and structurally junior to all indebtedness and other liabilities (including trade payables) of our subsidiaries.

Refer to Note 10 in our consolidated financial statements for other details, including our future minimum payments under the 2027 Notes.

Loan and Security Agreement

In November 2021, we entered into the Loan Agreement, by and among (i) U.S. Bank National Association, in its capacity as administrative agent (in such capacity, the Administrative Agent), and collateral agent (in such capacity, the Collateral Agent), (ii) certain lenders, or the Lenders, (iii) BridgeBio, as a borrower, and (iv) certain subsidiaries of BridgeBio, as guarantors, or the Guarantors.

Pursuant to the original terms and conditions of the Loan Agreement, the Lenders agreed to extend term loans to us in an aggregate principal amount of up to $750.0 million, comprised of (i) a tranche 1 advance of $450.0 million, or the Tranche 1 Advance, and (ii) a tranche 2 advance of $300.0 million, or the Tranche 2 Advance or collectively, the Term Loan Advances. The Tranche 1 Advance under the Loan Agreement was funded on November 17, 2021. The Tranche 2 Advance remained available for funding until December 31, 2022, which was available at our election after the occurrence of certain milestone events relating to data from our clinical trials. The terms related to the Tranche 2 Advance were modified in the First Amendment and Second Amendment as further discussed below. The First Amendment included the reduction of the aggregate amount of the Tranche 2 Advance from $300.0 million to $100.0 million. The Second Amendment eliminated the $100.0 million Tranche 2 Advance. As a result of the Second Amendment, the total aggregate principal amount of the loan is $450.0 million before any mandatory prepayment.

As security for our obligations under the Loan Agreement, each of BridgeBio and the Guarantors granted the Collateral Agent, for the benefit of the Lenders, a continuing security interest in substantially all of the assets of BridgeBio and the Guarantors, (including all equity interests owned or hereafter acquired by BridgeBio and the Guarantors), subject to certain customary exceptions. Upon exceeding certain investment and disposition thresholds, additional subsidiaries of BridgeBio will be required to join as guarantors.

Any outstanding principal on the Term Loan Advances will accrue interest at a fixed rate equal to 9.0% per annum, 3.0% of which can be paid in kind, or PIK, until January 1, 2025. Interest payments are payable quarterly following the funding of a Term Loan Advance. We will be required to make principal payments on the outstanding balance of the Term Loan Advances commencing on January 2, 2025, or the Term Loan Amortization Date in nine quarterly installments, plus interest. If we have achieved certain milestone events relating to data from the clinical trial of acoramidis, or the Acoramidis Milestone, on or prior to January 1, 2025, then the Term Loan Amortization Date will be automatically extended to January 2, 2026. Any amounts outstanding under the Term Loan Advances are due and payable on November 17, 2026, or the Maturity Date.

We may prepay the outstanding principal amount of the Term Loan Advances at any time (in whole, but not in part), plus accrued and unpaid interest and a prepayment premium ranging from 1.0% to 3.0% of the principal amount outstanding depending on the timing of payment (plus a customary make-whole amount if prepaid on or prior to November 17, 2022).

At the Lenders' election, we are also required to make mandatory prepayments upon the occurrence of certain prepayment events related to the repurchase or redemption of pledged collateral, entry into certain royalty transactions, disposition of other assets or subsidiaries, and entry into licensing and other monetization transactions (all such events "prepayment events"), which could be 50% or 75% of net cash proceeds from such transaction depending on achievement of the Acoramidis Milestone.

Subject to the mandatory prepayment requirements for certain prepayment events, the Loan Agreement contains customary affirmative and limited negative covenants which, among other things, limit our ability to (i) incur additional indebtedness, (ii) pay dividends or make certain distributions, (iii) dispose of our assets, grant liens, license or encumber our assets or (iv) fundamentally alter the nature of our business. BridgeBio and the Guarantors have broad ability to license our intellectual property, dispose of other assets and enter into monetization and royalty transactions, subject in each case to the requirement to make a mandatory prepayment described above. The Loan Agreement provides that BridgeBio and the Guarantors may, subject to certain limitations, (x) repurchase the BridgeBio’s equity interest and the equity interest of any of its subsidiaries, (y) enter into any joint ventures or similar investments, and (z) make other investments and acquisitions. Subject to the mandatory prepayment requirement described above, portfolio companies owned by BridgeBio that are not parties to the Loan Agreement are, subject to certain exceptions, not subject to any covenants or limitations under the Loan Agreement.

The Loan Agreement also contains customary events of default, including among other things, our failure to make any principal or interest payments when due, the occurrence of certain bankruptcy or insolvency events or the breach of the covenants under the Loan Agreement. Upon the occurrence of an event of default, the Lenders may, among other things, accelerate our obligations under the Loan Agreement.

We received net proceeds from the Tranche 1 Advance of $431.3 million, after deducting debt discount and issuance costs of $18.7 million, of which approximately $1.1 million of debt issuance cost were incurred for professional services provided by KKR Capital Markets LLC. KKR Capital Markets LLC is an affiliate of KKR Genetic Disorder L.P., a related party being a principal stockholder of BridgeBio.

In May 2022, we entered into the First Amendment, which, among other things:

- permitted the sale of our priority review voucher, or PRV, (see Note 12) and, generally, future dispositions of other PRVs;
- reduced the aggregate amount of the Tranche 2 Advance from $300.0 million to $100.0 million and modified certain conditions to the availability thereof, as mentioned above;
- amended the principal payments such that the entire outstanding principal balance of the Term Loan Advances is due and payable at the Maturity Date or upon early termination; and
- modified the terms and conditions governing when certain entities into which we have made investments will be required to become guarantors under the Amended Loan Agreement.

In June 2022, the receipt of an upfront payment under the Navire-BMS License Agreement, which is further described in Note 11, triggered certain mandatory prepayment provisions of the Amended Loan Agreement. As a result, we paid $20.5 million to the Lenders, of which $20.1 million and $0.4 million were applied to principal and exit fee, respectively.

Pursuant to the terms of the Loan Agreement and the Amended Loan Agreement, we exercised our option to convert accrued interest into principal via PIK amounting to $15.3 million and nil for the years ended December 31, 2022 and 2021, respectively.

In November 2022, we entered into the Second Amendment, which, among other things:

- acknowledged that the Company's prior prepayment made with certain cash proceeds received in connection with the receipt of an upfront payment under the Navire-BMS License Agreement, which is further described in Note 11, satisfied the mandatory prepayment requirement under the Amended Loan Agreement, on the terms and conditions specified in the Amended Loan Agreement;
- permitted certain budgeted expenses to be excluded from the definition of cash proceeds subject to the Company's mandatory prepayment obligations, on the terms and conditions specified in the Amended Loan Agreement; refer to Note 2 under Restricted Cash section for further discussion.
- removed certain threshold amounts applicable to certain prepayment events; and
- terminated the Lenders' $100.0 million Tranche 2 Advance.

Refer to Note 10 in our consolidated financial statements for other details, including our future minimum payments under the Loan Agreement.

Cash Flows

The following table summarizes our cash flows during the periods indicated:

	Year Ended December 31, 2022	2021	Change
	(in thousands)		
Net cash used in operating activities	$ (419,494)	$ (497,934)	$ 78,440
Net cash provided by (used in) investing activities	453,147	(200,826)	653,973
Net cash (used in) provided by financing activities	(13,134)	736,446	(749,580)
Net increase in cash, cash equivalents and restricted cash	$ 20,519	$ 37,686	$ (17,167)

Net Cash Flows Used in Operating Activities

Net cash used in operating activities was $419.5 million in 2022, consisting primarily of our net loss of $484.7 million, adjusted for non-cash items including a $110.0 million gain from the sale of our PRV (excluding transaction costs), $91.6 million in stock-based compensation expense, $13.6 million of payment-in-kind interest added to the term loan principal, $12.7 million in impairment of long-lived assets, $12.5 million gain from recognition of a receivable from Helsinn under the Amended QED-Helsinn License and Collaboration Agreement, $8.6 million debt accretion, $8.2 million in net loss from certain investment in equity securities, $6.8 million in depreciation and amortization, $6.3 million loss on the sale certain of assets in connection with the Origin-Sentynl APA, $5.2 million in noncash lease expense and $4.6 million fair value of shares issued under the license agreement, as well as $28.1 million net cash inflow related to changes in operating assets and liabilities. The $28.1 million net cash inflow related to changes in operating assets and liabilities was attributed mainly to an increase of $15.3 million in deferred revenue arising from the Navire-BMS License Agreement, decrease of $15.2 million in receivables from licensing and collaborative agreements, and decrease in other assets of $11.0 million, partially offset by a decrease of $5.0 million in accrued professional services, $4.3 million decrease in accrued research and development liabilities, $2.7 million decrease in other accrued and other long-term liabilities and decrease of $2.4 million in accrued compensation and benefits mainly due to timing of payments.

Net cash used in operating activities was $497.9 million in 2021, consisting primarily of our net loss of $586.5 million, adjusted for non-cash items including $99.5 million in stock-based compensation expense, $29.9 million in net gains from investment in equity securities, $5.8 million in depreciation and amortization, $5.8 million in accretion of debt, $5.6 million in noncash lease expense and $5.6 million of income from the derecognition of the LEO Call Option liability, as well as $4.4 million net cash outflow related to changes in operating assets and liabilities. The $4.4 million net cash outflow related to changes in operating assets and liabilities was attributed mainly to an increase of $19.7 million in receivable from licensing and collaboration agreements, an increase of $9.8 million in other assets and a decrease of $6.1 million in operating lease liabilities, partially offset by an increase of $12.0 million in other accrued and other long-term liabilities, an increase of $11.2 million in accrued research and development liabilities and an increase of $7.4 million in accrued compensation and benefits.

Net Cash Flows Provided by (Used in) Investing Activities

Net cash provided by investing activities was $453.1 million in 2022, consisting primarily of $479.7 million in maturities of marketable securities, $110.0 million gross proceeds from sale of PRV, $52.8 million in sale of investment in equity securities and $10.0 million proceeds from sale of certain assets, partially offset by $137.5 million purchases of marketable securities and $55.6 million purchases of investment in equity securities.

Net cash used in investing activities was $200.8 million in 2021, consisting primarily of purchases of marketable securities of $589.9 million, purchases of investment in equity securities of $53.4 million, acquisition of intangible assets of $35.0 million and purchases of property and equipment of $13.2 million, partially offset by $380.2 million and $62.7 million in maturities and sale, respectively, of marketable securities, $34.2 million in sale of investment in equity securities and $13.7 million increase in cash and cash equivalents from consolidation of PellePharm.

Cash Flows (Used in) Provided by Financing Activities

Net cash used in financing activities was $13.1 million in 2022, consisting primarily of prepayment of term loan of $20.5 million partially offset by net proceeds from the issuance of our common stock through ATM offering of $4.9 million.

Net cash provided by financing activities was $736.4 million in 2021, consisting primarily of net proceeds from the issuance of our 2029 Notes of $731.4 million, from net borrowings under our term loans of $456.3 million and from stock option exercises of $16.6 million, partially offset by repurchases of our common stock of $200.0 million, prepayments of the Amended Hercules Term Loan and the Tranche A loan aggregating to $124.1 million and purchase of capped calls of $61.3 million. We also used cash of $85.1 million to repurchase the noncontrolling interest of Eidos and pay for related direct transaction costs.

Critical Accounting Policies and Estimates

Our management's discussion and analysis of our financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with generally accepted accounting principles in the United States, or U.S. GAAP. The preparation of these consolidated financial statements requires us to make estimates and assumptions that affect the reported amounts of assets, liabilities, and the disclosure of contingent assets and liabilities at the date of the consolidated financial statements, as well as revenues and expenses incurred during the reporting periods. Our estimates are based on our historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

We believe that the following accounting policies are those most critical to the judgments and estimates used in the preparation of our consolidated financial statements for the periods in this report.

Collaborative Arrangements

We enter into collaboration arrangements with partners, under which we may grant licenses to further develop, manufacture and commercialize our drug compounds and or/products. We may also perform research, development, manufacturing, commercialization, and supply activities under our collaboration agreements. Consideration under these arrangements may include, upfront payments, development and regulatory milestones, expense reimbursements, royalties based on net sales of commercial products, and commercial sales milestone payments.

When we enter into collaboration agreements, we assess whether the arrangements fall within the scope of Accounting Standards Codification ("ASC") 808, *Collaborative Arrangements,* based on whether the arrangements involve joint operating activities and whether both parties have active participation in the arrangement and are exposed to significant risks and rewards. To the extent that the arrangement falls within the scope of ASC 808, we assess whether the payments between us and our partner fall within the scope of other accounting literature. If we conclude that payments from the partner to us represent consideration from a customer, such as license fees, contract manufacturing, and research and development activities, we account for those payments within the scope of ASC 606, *Revenue from Contracts with Customers*. However, if we conclude that our partner is not a customer for certain activities and associated payments, such as for certain collaborative research, development, manufacturing, and commercial activities, we record such payments as a reduction of research and development expense or selling, general and administrative expense, based on where we present the underlying expense. Additionally, if we reimburse our collaboration partners for these activities, we record such reimbursements as research and development expense or selling, general and administrative expense, depending upon the nature of the underlying expense.

If our collaborative arrangement provides for the sharing of profits and losses with our partner for commercialization activities, the treatment of our share in the profit-sharing structure depends on who the selling party is. If we are the selling party and the deemed principal, we record our collaboration partner's share of profits as an addition to selling, general and administrative expenses and our collaboration partner's share of loss as a reduction in selling, general and administrative expenses. If our partner is the selling party and the deemed principal, we record our share of profits as collaboration revenue and our share of losses as an addition to selling, general and administrative expenses.

Revenue Recognition

For elements or transactions that we determine should be accounted for under ASC 606, we perform the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) we satisfy our performance obligation. We apply the five-step model to contracts when it is probable that we will collect the consideration to which we are entitled in exchange for the goods or services we transfer to the customer.

At inception of the arrangement, we assess the promised goods or services to identify the performance obligations within the contract. We then recognize as revenue the amount of the transaction price that is allocated to the respective performance obligation, on a relative standalone selling price basis, when (or as) the performance obligation is satisfied, either at a point in time or over time. If the performance obligation is satisfied over time, we recognize revenue based on the use of an input method. As part of the accounting for these arrangements, we develop assumptions that require judgment to determine the standalone selling price for each performance obligation identified in the contract. These key assumptions may include forecasted revenue or costs, development timelines, discount rates and probabilities of clinical and regulatory success.

License Fees: For arrangements that include a grant of a license to our intellectual property, we consider whether the license grant is distinct from the other performance obligations included in the arrangement. Generally, we would conclude that the license is distinct if the customer is able to benefit from the license with the resources available to it. For licenses that are distinct, we recognize revenues from nonrefundable, upfront license fees and other consideration allocated to the license when the license term has begun and we have provided all necessary information regarding the underlying intellectual property to the customer, which generally occurs at or near the inception of the arrangement. For licenses that are bundled with other promises, we determine whether the combined performance obligation is satisfied over time or at a point in time. If the combined performance obligation is satisfied over time, we use judgment in determining the appropriate method of measuring progress for purposes of recognizing revenue from the up-front license fees. We evaluate the measure of progress each reporting period and, if necessary, adjust the measure of performance and related revenue recognition.

Development and Regulatory Milestone Payments: At the inception of each arrangement that includes development and regulatory milestone payments, we evaluate whether the milestones are considered probable of being achieved and estimate the amount to be included in the transaction price using the most likely amount method. We generally include these milestone payments when they are achieved because there is considerable uncertainty in the research and development processes that trigger these payments under our agreements. Similarly, we include approval milestone payments in the transaction price once the product is approved by the applicable regulatory agency. At the end of each subsequent reporting period, we re-evaluate the probability of achieving such development and regulatory milestones and any related constraint, and if necessary, adjust our estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis.

Sales-based Milestone Payments and Royalties: For arrangements that include sales-based royalties, including milestone payments based on the volume of sales, we will determine whether the license is deemed to be the predominant item to which the royalties or sales-based milestones relate and if such is the case, we will recognize revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied).

Product supply services: Arrangements that include a promise for the future supply of drug product for either clinical development or commercial supply at the licensee's discretion are generally considered as options. We will assess if these options provide a material right to the licensee and if so, they are accounted for as separate performance obligations and recognized when the future goods or services related to the option are provided or the option expires.

Research and Development Services: For arrangements that include research and development services, we will recognize revenue over time using an input method, representing the transfer of goods or services as we perform activities over the term of the agreement.

Accrued Research and Development Liabilities

We record accruals for estimated costs of research and development activities conducted by third-party service providers, which include the conduct of preclinical studies, clinical trials, and contract manufacturing activities. We record the estimated costs of research and development activities based upon the estimated amount of services provided but not yet invoiced, and include these costs in accrued research and development liabilities in the consolidated balance sheets and within research and development expense in the consolidated statements of operations. These costs are a significant component of our research and development expenses.

Examples of estimated research and development expenses that we accrue include:

- fees paid to CROs in connection with preclinical and toxicology studies and clinical trials;
- fees paid to investigative sites in connection with clinical trials;
- fees paid to CMOs in connection with the production of product and clinical trial materials; and
- professional service fees for consulting and related services.

We base our expense accruals related to clinical trials on our estimates of the services received and efforts expended pursuant to contracts with multiple research institutions and CROs that conduct and manage clinical trials on our behalf. The financial terms of these agreements vary from contract to contract and may result in uneven payment flows. Payments under some of these contracts depend on factors, such as the successful enrollment of patients and the completion of clinical trial milestones. Our service providers generally invoice us monthly in arrears for services performed. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If we do not identify costs that we have begun to incur or if we underestimate or overestimate the level of services performed or the costs of these services, our actual expenses could differ from our estimates. We record advance payments to service providers as prepaid assets.

We record accruals for the estimated costs of our contract manufacturing activities performed by third parties. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows to our vendors. Payments under the contracts include upfront payments and milestone payments, which depend on factors such as the achievement of the completion of certain stages of the manufacturing process. For purposes of recognizing expense, we assess whether we consider the production process sufficiently defined to be considered the delivery of a good or the delivery of a service, where processes and yields are developing and less certain. If we consider the process to be the delivery of a good, we recognize expense when the drug product is delivered, or we otherwise bear risk of loss. If we consider the process to be the delivery of a service, we recognize expense based on our best estimates of the contract manufacturer's progress towards completion of the stages in the contract. We base our estimates on the best information available at the time. However, additional information may become available to us which may allow us to make a more accurate estimate in future periods. In this event, we may be required to record adjustments to research and development expenses in future periods when the actual level of activity becomes more certain. Any increases or decreases in cost are generally considered to be changes in estimates and will be reflected in research and development expenses in the period identified.

To date, we have not experienced significant changes in our estimates of accrued research and development liabilities after a reporting period. However, due to the nature of estimates, there is no assurance that we will not make changes to our estimates in the future as we become aware of additional information about the status or conduct of our clinical studies and other research activities.

Accrued Milestone Compensation Arrangements

We have performance-based milestone compensation arrangements with certain employees and consultants, whose vesting is contingent upon meeting various regulatory and development milestones, with fixed monetary amounts known at inception that can be settled in the form of (i) cash, (ii) equity of BridgeBio, or (iii) cash or equity of BridgeBio at our sole election, upon achievement of each contingent milestone. For arrangements that involve settlement by cash or equity of BridgeBio at our sole election, we will classify the milestone compensation arrangements as liability-classified awards when it is probable of achievement because of the possible fixed monetary amounts settlement outcomes. The arrangements would also result in settlement with a variable number of shares based on the then-current stock price at achievement date of each contingent milestone should we elect to settle in equity.

We record accruals for the compensation expense arising from each development milestone when the specific contingent development milestone is probable of achievement and such accruals are measured at each reporting period. We estimate the probability of achieving such milestones based on the progression and expected outcome of the related clinical programs. We base our estimates on the best available information at that time. However, additional information may become available to us which may allow us to make a more accurate estimate in future periods. In this event, we may be required to record adjustments to milestone compensation expenses in future periods. Any increases or decreases in such expenses are generally considered to be changes in estimates and will be reflected in the period identified.

To date, we have not experienced significant changes in our estimates of accrued milestone compensation expenses after a reporting period. However, due to the nature of estimates, there is no assurance that we will not make changes to our estimates in the future as we become aware of additional information about the progression and expected outcome of our clinical programs.

Recent Accounting Pronouncements

See Note 2, “Summary of Significant Accounting Policies - Recently Adopted Accounting Pronouncements” to our consolidated financial statements appearing under Part II, Item 8 for more information.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

As of December 31, 2022 and 2021, we held cash, cash equivalents, marketable securities and restricted cash of $466.2 million and $787.7 million, respectively. Our cash equivalents consist of amounts invested in money market accounts, such as money market funds and short-term commercial paper. Our marketable securities consist of high investment grade fixed income securities that are primarily invested in commercial paper, corporate bonds, and U.S. government securities. We do not enter into investments for trading or speculative purposes and have not used any derivative financial instruments to manage our interest rate risk exposure. We have not been exposed nor do we anticipate being exposed to material risks due to changes in interest rates. We do not believe that our cash, cash equivalents or marketable securities have a significant risk of default or illiquidity.

As of December 31, 2022, we had no outstanding debt with a variable interest rate. Our 2029 Notes, 2027 Notes and term loan had principal balances of $747.5 million, $550.0 million and $445.2 million, respectively, as of December 31, 2022, and bear fixed interest rates. As of December 31, 2021, we had no outstanding debt with a variable interest rate. Our 2029 Notes, 2027 Notes and term loan had principal balances of $747.5 million, $550.0 million and $450.0 million, respectively, as of December 31, 2021, and bear fixed interest rates. Our cash flows on these debt obligations are not subject to variability as a result of changes in interest rates. A hypothetical 100 basis point change in interest rate during any of the periods presented would not have had a material impact on our financial statements.

We are exposed to changes in the fair value of our investments in equity securities. As of December 31, 2022, our investment in equity securities, which consist of equity securities of publicly held companies, have a balance of $43.7 million. These shares are carried in our consolidated balance sheet at fair value based on the closing price of the shares owned on the last trading day of the reporting period. Fluctuations in the underlying bid price of the shares could result in material gains or losses. As of December 31, 2021, our investment in equity securities, which consist of equity securities of publicly held companies, had a balance of $49.1 million. These shares are carried in our consolidated balance sheet at fair value based on the closing price of the shares owned on the last trading day of the reporting period.

We do not believe that inflation and changing prices had a significant impact on our business, financial conditions or results of operations for any of the periods presented herein. Significant adverse changes in inflation and prices in the future could result in material losses.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Shareholders and the Board of Directors of BridgeBio Pharma, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of BridgeBio Pharma, Inc., its subsidiaries and controlled entities (the “Company”) as of December 31, 2022 and 2021, the related consolidated statements of operations, comprehensive loss, redeemable convertible noncontrolling interests and shareholders’ equity (deficit), and cash flows, for each of the three years in the period ended December 31, 2022, and the related notes (collectively referred to as the “financial statements”). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2022 and 2021, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2022, in conformity with accounting principles generally accepted in the United States of America.

We have also audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the Company’s internal control over financial reporting as of December 31, 2022, based on criteria established in *Internal Control — Integrated Framework (2013)* issued by the Committee of Sponsoring Organizations of the Treadway Commission and our report dated February 23, 2023, expressed an unqualified opinion on the Company’s internal control over financial reporting.

Basis for Opinion

These financial statements are the responsibility of the Company’s management. Our responsibility is to express an opinion on the Company’s financial statements based on our audits. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the US federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

Critical Audit Matter

The critical audit matter communicated below is a matter arising from the current-period audit of the financial statements that was communicated or required to be communicated to the audit committee and that (1) relates to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective, or complex judgments. The communication of critical audit matters does not alter in any way our opinion on the financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing a separate opinion on the critical audit matter or on the accounts or disclosures to which it relates.

Research and Development Expenses and Accrued Research and Development Liabilities - Refer to Notes 2 and 9 to the financial statements

Critical Audit Matter Description

The Company incurs research and development expenses related to the costs of research and development activities, including third-party service agreements with contract research organizations (CROs) and contract manufacturing organizations (CMOs) to provide research and development services related to preclinical studies and clinical trials, which are estimated at each reporting period. As of December 31, 2022, the Company had accrued for $40 million of research and development expenses, of which $34 million is related to CROs and CMOs. In addition, the Company's total prepaid expenses and other current assets were $22 million and other assets were $20 million, which included $7 million and $10 million, respectively, for amounts paid in advance of services incurred to be performed by CROs and CMOs. The Company incurred $399 million of research and development expenses for the year ended December 31 2022, of which $150 million is related to services provided by CROs and CMOs. The Company records these expenses based on estimates of the services and activities completed to date pursuant to the provisions of the signed contracts relative to the amounts invoiced and paid to date, resulting in an accrued liability or prepaid expense balance at period-end.

We identified the accrual of these third-party research and development costs as a critical audit matter because of the judgments necessary for management to estimate the cost of services provided but not yet invoiced, the significant volume of transactions and the varied nature of audit evidence obtained from vendor to vendor. The amount of expense recognized and the corresponding accrual and prepaid balances recorded are based on the unique terms and conditions in each arrangement and are often dependent on limited information available from the vendors regarding the progress of the services through the reporting date. This required extensive audit effort due to the volume and variability in the arrangements and available information from the vendors and required a high degree of auditor judgment when performing audit procedures to audit management's estimates of total expenses, accrued and prepaid balances and evaluating the results of those procedures.

How the Critical Audit Matter Was Addressed in the Audit

Our audit procedures related to the estimate of research and development expenses and the related accrued and prepaid balances included the following, among others:

- We evaluated the design and tested the operating effectiveness of controls over the Company's research and development expense accrual process, including controls over the estimation of activities completed to date.
- We evaluated publicly available information (e.g., the Company's website, news, articles, press releases, and investor presentations) and Board of Directors' materials, and corroborated this information gathered with Company personnel responsible for overseeing the clinical trial activities regarding the status of such activities. We then compared this information to the judgements applied in management's estimate of the recorded expenses and corresponding accrual and prepaid balances.
- We evaluated management's ability to accurately estimate accrual of these third-party research and development costs by performing a lookback analysis, comparing actual results to management's historical estimates.
- For a sample of contracts, we evaluated the third-party research and development expenses and the corresponding accrued and prepaid expense balances by:

    — inspecting related agreements, including (but not limited to) master service agreements, change orders, statements of work, and amendments, and agreeing key provisions of the agreements, including timeline, budget, and relevant rates, to the Company's analysis of estimated expenses incurred to date.

— sending written confirmations directly to CROs or CMOs to confirm completeness of agreements as well as payments received, invoices billed and yet to be billed, and costs incurred to date and inspecting correspondence received directly from them, including status reports, and comparing such information to the amounts used in the Company's estimates.

— agreeing other third-party information to the inputs used in the Company's analysis and recalculating the Company's estimated expense, accrual, and prepaid balances.

— performing a lookback analysis by comparing the estimated accrual balance as of December 31, 2021, to the invoices received after December 31, 2021 to evaluate the Company's ability to estimate the accrual.

/s/ Deloitte & Touche LLP

San Francisco, California
February 23, 2023

We have served as the Company's auditor since 2018.

BRIDGEBIO PHARMA, INC.
Consolidated Balance Sheets
(in thousands, except shares and per share amounts)

	December 31, 2022	December 31, 2021
Assets		
Current assets:		
Cash and cash equivalents	$ 376,689	$ 393,772
Marketable securities	51,580	393,743
Investment in equity securities	43,653	49,148
Receivable from licensing and collaboration agreements	17,079	19,749
Restricted cash	37,930	177
Prepaid expenses and other current assets	21,922	32,269
Total current assets	548,853	888,858
Property and equipment, net	14,569	30,066
Operating lease right-of-use assets	10,678	15,907
Intangible assets, net	28,712	44,934
Other assets	20,224	33,027
Total assets	$ 623,036	$ 1,012,792
Liabilities, Redeemable Convertible Noncontrolling Interests and Stockholders' Deficit		
Current liabilities:		
Accounts payable	$ 11,558	$ 11,884
Accrued compensation and benefits	31,256	37,041
Accrued research and development liabilities	39,803	44,138
Accrued professional services	1,790	6,786
Operating lease liabilities, current portion	3,675	4,938
Deferred revenue, current portion	8,156	—
Other accrued liabilities	25,190	30,282
Total current liabilities	121,428	135,069
2029 Notes, net	734,988	733,119
2027 Notes, net	541,634	539,934
Term loan, net	430,993	430,752
Operating lease liabilities, net of current portion	12,274	17,428
Other long-term liabilities	26,643	22,069
Total liabilities	1,867,960	1,878,371
Commitments and contingencies (Note 9)		
Redeemable convertible noncontrolling interests	(1,589)	1,423
Stockholders' deficit:		
Undesignated preferred stock, $0.001 par value; 25,000,000 shares authorized; no shares issued and outstanding	—	—
Common stock, $0.001 par value; 500,000,000 shares authorized; 156,817,333 shares issued and 150,625,572 shares outstanding as of December 31, 2022, 153,535,084 shares issued and 147,343,323 shares outstanding as of December 31, 2021	157	154
Treasury stock, at cost; 6,191,761 shares as of December 31, 2022 and 2021	(275,000)	(275,000)
Additional paid-in capital	938,703	841,530
Accumulated other comprehensive loss	(328)	(132)
Accumulated deficit	(1,918,149)	(1,436,966)
Total BridgeBio stockholders' deficit	(1,254,617)	(870,414)
Noncontrolling interests	11,282	3,412
Total stockholders' deficit	(1,243,335)	(867,002)
Total liabilities, redeemable convertible noncontrolling interests and stockholders' deficit	$ 623,036	$ 1,012,792

The accompanying notes are an integral part of these consolidated financial statements.

BRIDGEBIO PHARMA, INC.
Consolidated Statements of Operations
(in thousands, except shares and per share amounts)

	Year Ended December 31,		
	2022	2021	2020
Revenue:			
License and services revenue	$ 76,094	$ 65,923	$ 8,249
Product sales	1,554	3,793	—
Total revenue	77,648	69,716	8,249
Operating costs and expenses:			
Cost of license revenue and products sold	3,434	3,114	—
Research and development	399,462	451,024	337,047
Selling, general and administrative	143,189	192,210	145,684
Restructuring, impairment and related charges	43,765	—	—
Total operating costs and expenses	589,850	646,348	482,731
Loss from operations	(512,202)	(576,632)	(474,482)
Other income (expense), net:			
Interest income	7,542	1,133	4,015
Interest expense	(80,438)	(46,778)	(36,655)
Gain from sale of priority review voucher, net	107,946	—	—
Other income (expense), net	(7,500)	35,823	1,634
Total other income (expense), net	27,550	(9,822)	(31,006)
Net loss	(484,652)	(586,454)	(505,488)
Net loss attributable to redeemable convertible noncontrolling interests and noncontrolling interests	3,469	23,915	56,764
Net loss attributable to common stockholders of BridgeBio	$ (481,183)	$ (562,539)	$ (448,724)
Net loss per share attributable to common stockholders of BridgeBio, basic and diluted	$ (3.26)	$ (3.90)	$ (3.80)
Weighted-average shares used in computing net loss per share attributable to common stockholders of BridgeBio, basic and diluted	147,473,076	144,356,619	117,995,457

The accompanying notes are an integral part of these consolidated financial statements.

BRIDGEBIO PHARMA, INC.
Consolidated Statements of Comprehensive Loss
(in thousands)

	Year Ended December 31,		
	2022	2021	2020
Net loss	$ (484,652)	$ (586,454)	$ (505,488)
Other comprehensive loss:			
Unrealized loss on available-for-sale securities	(196)	(324)	(62)
Comprehensive loss	(484,848)	(586,778)	(505,550)
Comprehensive loss attributable to redeemable convertible noncontrolling interests and noncontrolling interests	3,469	23,915	56,764
Comprehensive loss attributable to common stockholders of BridgeBio	$ (481,379)	$ (562,863)	$ (448,786)

The accompanying notes are an integral part of these consolidated financial statements.

BRIDGEBIO PHARMA, INC.
Consolidated Statements of Redeemable Convertible Noncontrolling Interests and Stockholders’ Equity (Deficit)
(in thousands, except shares and per share amounts)

	Redeemable Convertible Noncontrolling Interests	Common Stock Shares	Common Stock Amount	Treasury Stock Shares	Treasury Stock Amount	Additional Paid-In Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total BridgeBio Stockholders' Equity (Deficit)	Noncontrolling Interests	Total Stockholders’ Equity (Deficit)
Balances as of December 31, 2019	$ 2,243	123,658,287	$ 124	—	$ —	$ 848,107	$ 254	$ (440,031)	$ 408,454	$ 65,279	$ 473,733
Issuance of shares under equity compensation plans	—	919,502	—	—	—	3,711	—	—	3,711	—	3,711
Issuance of shares under the 2020 Stock and Equity Award Exchange Program	—	655,719	1	—	—	1,673	—	—	1,674	(1,674)	—
Stock-based compensation	—	—	—	—	—	36,530	—	—	36,530	—	36,530
Equity component of 2027 Notes, net of issuance costs and deferred tax liability	—	—	—	—	—	168,078	—	—	168,078	—	168,078
Purchase of capped calls	—	—	—	—	—	(49,280)	—	—	(49,280)	—	(49,280)
Repurchase of common stock	—	(2,414,681)	—	2,414,681	(75,000)	—	—	—	(75,000)	—	(75,000)
Issuance of common stock under ESPP	—	49,696	—	—	—	1,205	—	—	1,205	—	1,205
Repurchase of common stock to satisfy tax withholding	—	(19,134)	—	—	—	(714)	—	—	(714)	—	(714)
Unrealized loss on available-for-sale securities	—	—	—	—	—	—	(62)	—	(62)	—	(62)
Issuance (repurchase) of noncontrolling interest	2,102	—	—	—	—	—	—	—	—	50,828	50,828
Transfers from (to) noncontrolling interest	1,843	—	—	—	—	12,034	—	—	12,034	(13,877)	(1,843)
Net loss	(4,558)	—	—	—	—	—	—	(448,724)	(448,724)	(52,206)	(500,930)
Balances as of December 31, 2020	1,630	122,849,389	125	2,414,681	(75,000)	1,021,344	192	(888,755)	57,906	48,350	106,256
Cumulative effect of ASU 2020-06 adoption	—	—	—	—	—	(168,078)	—	14,328	(153,750)	—	(153,750)
Repurchase of Eidos noncontrolling interests for cash and shares, including transaction costs of $70,734	—	26,156,446	26	—	—	(53,856)	—	—	(53,830)	(38,167)	(91,997)
Purchase of capped calls	—	—	—	—	—	(61,295)	—	—	(61,295)	—	(61,295)
Fair value of PellePharm noncontrolling interest on consolidation	5,074	—	—	—	—	—	—	—	—	—	—
Repurchase of common stock	—	(3,777,080)	—	3,777,080	(200,000)	—	—	—	(200,000)	—	(200,000)
Issuance of shares under equity compensation plans	—	2,085,286	3	—	—	16,642	—	—	16,645	—	16,645
Stock-based compensation	—	—	—	—	—	89,823	—	—	89,823	—	89,823
Issuance of common stock under ESPP	—	116,222	—	—	—	3,821	—	—	3,821	—	3,821
Repurchase of common stock to satisfy tax withholding	—	(86,940)	—	—	—	(4,747)	—	—	(4,747)	—	(4,747)
Unrealized losses on available-for-sale securities	—	—	—	—	—	—	(324)	—	(324)	—	(324)
Issuance (repurchase) of noncontrolling interest	3,500	—	—	—	—	—	—	—	—	6,240	6,240
Transfers from (to) noncontrolling interests	(3,456)	—	—	—	—	(2,124)	—	—	(2,124)	5,579	3,455
Net loss	(5,325)	—	—	—	—	—	—	(562,539)	(562,539)	(18,590)	(581,129)
Balances as of December 31, 2021	1,423	147,343,323	154	6,191,761	(275,000)	841,530	(132)	(1,436,966)	(870,414)	3,412	(867,002)
Issuance of shares under equity compensation plans	—	2,658,109	3	—	—	663	—	—	666	—	666
Repurchase of common stock to satisfy tax withholding	—	(171,209)	—	—	—	(1,561)	—	—	(1,561)	—	(1,561)
Stock-based compensation	—	—	—	—	—	94,173	—	—	94,173	—	94,173
Issuance of common stock under ESPP	—	339,549	—	—	—	2,558	—	—	2,558	—	2,558
Issuance of common stock through at-the-market offering, net	—	455,800	—	—	—	4,852	—	—	4,852	—	4,852
Unrealized loss on available-for-sale securities	—	—	—	—	—	—	(196)	—	(196)	—	(196)
Issuance (repurchase) of noncontrolling interest	—	—	—	—	—	—	—	—	—	4,815	4,815
Transfers from (to) noncontrolling interest	2,399	—	—	—	—	(3,512)	—	—	(3,512)	1,113	(2,399)
Net loss	(5,411)	—	—	—	—	—	—	(481,183)	(481,183)	1,942	(479,241)
Balances as of December 31, 2022	$ (1,589)	150,625,572	$ 157	6,191,761	$ (275,000)	$ 938,703	$ (328)	$ (1,918,149)	$ (1,254,617)	$ 11,282	$ (1,243,335)

The accompanying notes are an integral part of these consolidated financial statements.

BRIDGEBIO PHARMA, INC.
Consolidated Statements of Cash Flows
(in thousands)

	Year Ended December 31,		
	2022	2021	2020
Operating activities			
Net loss	$ (484,652)	$ (586,454)	$ (505,488)
Adjustments to reconcile net loss to net cash used in operating activities:			
Stock-based compensation	91,559	99,505	58,459
Depreciation and amortization	6,771	5,843	1,456
Noncash lease expense	5,172	5,611	3,088
Net loss (gain) from investment in equity securities	8,222	(29,914)	—
Gain from sale of priority review voucher, excluding transaction costs	(110,000)	—	—
Accrual of payment-in-kind interest on term loan	13,562	—	—
Gain from recognition of receivable from licensing and collaboration agreement	(12,500)	—	—
Fair value of shares issued under license agreements	4,567	—	6,014
Accretion of debt	8,570	5,795	17,737
Fair value adjustment of warrants	1,571	1,197	(3,338)
Loss on sale of certain assets	6,261	—	—
Impairment of long-lived assets	12,720	—	—
LEO call option expense (income)	—	(5,550)	1,472
Loss on early extinguishment of debt	—	3,337	—
Acquired in-process research and development assets	—	—	4,727
Other noncash adjustments	604	7,092	1,225
Changes in operating assets and liabilities:			
Receivable from licensing and collaboration agreements	15,169	(19,749)	—
Receivable from a related party	—	—	2,845
Prepaid expenses and other current assets	7,671	(4,262)	(7,059)
Other assets	10,971	(9,816)	(2,146)
Accounts payable	(349)	2,833	(735)
Accrued compensation and benefits	(2,362)	7,378	8,589
Accrued research and development liabilities	(4,309)	11,178	6,170
Accrued professional services	(4,996)	2,157	2,407
Operating lease liabilities	(6,245)	(6,122)	(3,472)
Deferred revenue	15,262	—	—
Other accrued and other long-term liabilities	(2,733)	12,007	8,335
Net cash used in operating activities	(419,494)	(497,934)	(399,714)
Investing activities			
Purchases of marketable securities	(137,493)	(589,892)	(287,852)
Maturities of marketable securities	479,688	380,200	249,137
Sales of marketable securities	—	62,691	—
Purchases of investment in equity securities	(55,562)	(53,383)	—
Sales of investment in equity securities	52,835	34,150	—
Increase in cash and cash equivalents from consolidation of PellePharm	—	13,654	—
Payment for intangible assets	(1,500)	(35,000)	—
Proceeds from sale of priority review voucher, excluding transaction costs	110,000	—	—
Proceeds from sale of certain assets	10,000	—	—
Purchases of property and equipment	(4,821)	(13,246)	(7,518)
Other investing activities	—	—	(6,760)
Net cash provided by (used in) investing activities	453,147	(200,826)	(52,993)
Financing activities			
Proceeds from issuance of 2029 Notes in 2021 and 2027 Notes in 2020	—	747,500	550,000
Issuance costs and discounts associated with issuance of 2029 Notes and 2027 Notes	—	(16,064)	(13,039)
Purchase of capped calls	—	(61,295)	(49,280)
Repurchase of common stock	—	(200,000)	(75,000)
Proceeds from issuance of noncontrolling interests	—	3,500	2,000
Repurchase of Eidos noncontrolling interest, including direct transaction costs	—	(85,090)	—
Proceeds from term loan, net of issuance costs	—	456,296	—
Repayment of term loan	(20,486)	(124,119)	—
Proceeds from common stock issuances under ESPP	2,558	3,821	1,205
Repurchase of common stock to satisfy tax withholding	(1,561)	(4,746)	(714)
Proceeds from stock option exercises, net of repurchases	666	16,643	12,923
Proceeds from at-the-market issuance of noncontrolling interest by Eidos, net	—	—	24,094
Proceeds from issuance of common stock through at-the-market offering, net	4,852	—	—
Repurchase of noncontrolling interest	—	—	(5,000)
Other financing activities	837	—	—
Net cash (used in) provided by financing activities	(13,134)	736,446	447,189
Net increase (decrease) in cash, cash equivalents and restricted cash	20,519	37,686	(5,518)
Cash, cash equivalents and restricted cash at beginning of year	396,365	358,679	364,197
Cash, cash equivalents and restricted cash at end of year	$ 416,884	$ 396,365	$ 358,679

The accompanying notes are an integral part of these consolidated financial statements.

	Year Ended December 31,		
	2022	2021	2020
Supplemental Disclosures of Cash Flow Information:			
Cash paid for interest	$ 54,443	$ 29,774	$ 15,322
Supplemental Disclosures of Non-Cash Investing and Financing Information:			
Payment-in-kind interest accrued in prior year added to principal of term loan	$ 1,763	$ —	$ —
Deferred merger transaction costs included in accounts payable and accrued professional services	$ —	$ —	$ 1,842
Leasehold improvements paid by landlord	$ —	$ 2,449	$ —
Transfers from (to) noncontrolling interests (Note 6)	$ (3,512)	$ (2,124)	$ 12,034
Recognition of property and equipment previously classified in other assets	$ —	$ —	$ 10,000
Noncash contribution by a noncontrolling interest	$ —	$ 21,600	$ 4,727
Unpaid property and equipment	$ 47	$ 563	$ 1,101
Recognized intangible asset recorded in other accrued and other long-term liabilities	$ 11,000	$ 12,500	$ —
Unpaid debt issuance costs	$ —	$ 1,120	$ —
Net noncash portion of repurchase of Eidos noncontrolling interests	$ —	$ 38,168	$ —
Direct transaction costs in the repurchase of Eidos recorded in additional paid-in capital previously classified in prepaid expenses and other current assets	$ —	$ 8,749	$ —
Reconciliation of Cash, Cash Equivalents and Restricted Cash			
Cash and cash equivalents	$ 376,689	$ 393,772	$ 356,082
Restricted cash	37,930	177	139
Restricted cash - included in other assets	2,265	2,416	2,458
Total cash, cash equivalents and restricted cash at end of year	$ 416,884	$ 396,365	$ 358,679

The accompanying notes are an integral part of these consolidated financial statements.

1. Organization and Description of Business

BridgeBio Pharma, Inc. or BridgeBio or the Company, is a commercial-stage biopharmaceutical company founded to discover, create, test and deliver transformative medicines to treat patients who suffer from genetic diseases and cancers with clear genetic drivers. BridgeBio's pipeline of development programs ranges from early science to advanced clinical trials. BridgeBio was founded in 2015 and its team of experienced drug discoverers, developers and innovators are committed to applying advances in genetic medicine to help patients as quickly as possible.

Since inception, BridgeBio has either created wholly-owned subsidiaries or has made investments in certain controlled entities, including partially-owned subsidiaries for which BridgeBio has a majority voting interest, and variable interest entities, or VIEs for which BridgeBio is the primary beneficiary, or, collectively, we, our, or us. BridgeBio is headquartered in Palo Alto, California.

2. Summary of Significant Accounting Policies

Basis of Presentation and Principles of Consolidation

The consolidated financial statements include the accounts of BridgeBio Pharma, Inc., its wholly-owned subsidiaries and controlled entities, substantially all of which are denominated in U.S. dollars. All intercompany balances and transactions have been eliminated in consolidation. For consolidated entities where we own or are exposed to less than 100% of the economics, we record "Net loss attributable to redeemable convertible noncontrolling interests and noncontrolling interests" in our consolidated statements of operations equal to the percentage of the economic or ownership interests retained in such entities by the respective noncontrolling parties.

In determining whether an entity is considered a controlled entity, we applied the VIE and Voting Interest Entity, or VOE models. We assess whether we are the primary beneficiary of a VIE based on our power to direct the activities of the VIE that most significantly impact the VIE’s economic performance and our obligation to absorb losses or the right to receive benefits from the VIE that could potentially be significant to the VIE. Entities that do not qualify as a VIE are assessed for consolidation under the VOE model. Under the VOE model, BridgeBio consolidates the entity if it determines that it has a controlling financial interest in the entity through its ownership of greater than 50% of the outstanding voting shares of the entity and that other equity holders do not have substantive voting, participating or liquidation rights. We assess whether we are the primary beneficiary of a VIE or whether we have a majority voting interest for entities consolidated under the VOE model at the inception of the arrangement and at each reporting date.

The consolidated financial statements have been prepared in accordance with generally accepted accounting principles in the United States, or U.S. GAAP and, in the opinion of management, reflect all adjustments, which include only normal recurring adjustments, necessary for a fair statement of our financial position, our results of operations and comprehensive loss, and our cash flows for the periods presented. The results of operations for the years ended December 31, 2022, 2021 and 2020 are not necessarily indicative of the results to be expected for the year ending December 31, 2023 or for any other future annual or interim period.

Reclassifications

Certain reclassifications have been made to the consolidated statements of cash flows for the year ended December 31, 2020 to conform to the current year’s presentation. These reclassifications had no net effect on cash flows from operating, investing and financing activities as previously reported.

Variable Interest Entities and Voting Interest Entities

BridgeBio consolidates those entities in which it has a direct or indirect controlling financial interest based on either the VIE model or the VOE model.

VIEs are entities that, by design, either (i) lack sufficient equity to permit the entity to finance its activities without additional subordinated financial support from other parties; or (ii) have equity investors that do not have the ability to make significant decisions relating to the entity's operations through voting rights, or do not have the obligation to absorb the expected losses, or do not have the right to receive the residual returns of the entity.

The primary beneficiary of a VIE is required to consolidate the assets and liabilities of the VIE. The primary beneficiary is the party that has both (i) the power to direct the activities of the VIE that most significantly impact the VIE's economic performance, and (ii) the obligation to absorb losses or the right to receive benefits from the VIE that could potentially be significant to the VIE through its interest in the VIE.

To assess whether BridgeBio has the power to direct the activities of a VIE that most significantly impact the VIE's economic performance, BridgeBio considers all the facts and circumstances, including its role in establishing the VIE and its ongoing rights and responsibilities. This assessment includes identifying the activities that most significantly impact the VIE's economic performance and identifying which party, if any, has power over those activities. In general, the parties that make the most significant decisions affecting the VIE (management and representation on the Board of Directors) and have the right to unilaterally remove those decision-makers are deemed to have the power to direct the activities of a VIE.

To assess whether BridgeBio has the obligation to absorb losses of the VIE or the right to receive benefits from the VIE that could potentially be significant to the VIE, BridgeBio considers all of its economic interests, which primarily include equity investments in preferred and common stock and issuance of notes that are convertible into preferred stock, that are deemed to be variable interests in the VIE. This assessment requires BridgeBio to apply judgment in determining whether these interests, in the aggregate, are considered potentially significant to the VIE. Factors considered in assessing the significance include: the design of the VIE, including its capitalization structure, subordination of interests, payment priority, relative share of interests held across various classes within the VIE's capital structure, and the reasons why the interests are held by BridgeBio.

At the VIE's inception, BridgeBio determines whether it is the primary beneficiary and if the VIE should be consolidated based on the facts and circumstances. We have determined that the consolidated VIEs, in which BridgeBio is the primary beneficiary, individually meet the definition of a business. There are no significant restrictions on the assets and liabilities of BridgeBio's consolidated VIEs. BridgeBio then performs ongoing reassessments of the VIE based on reconsideration events and reevaluates whether a change to the consolidation and disclosure conclusions are required each reporting period.

Entities that do not qualify as a VIE are assessed for consolidation under the VOE model. Under the VOE model, BridgeBio consolidates the entity if it determines that it, directly or indirectly, has greater than 50% of the voting shares and that other equity holders do not have substantive voting, participating, or liquidation rights. Refer to Note 5.

Equity Method and Other Equity Investments

We utilize the equity method to account for investments when we possess the ability to exercise significant influence, but not control, over the operating and financial decisions of the investee. Generally, the ability to exercise significant influence is presumed when the investor possesses more than 20% of the voting interests of the investee. This presumption may be overcome based on specific facts and circumstances that demonstrate that the ability to exercise significant influence is restricted. We apply the equity method to investments in common stock and to other investments in entities that have risk and reward characteristics that are substantially similar to an investment in the investee's common stock.

In applying the equity method, we record the investment at cost unless the initial recognition is the result of the deconsolidation of a subsidiary, in which case it is recorded at fair value. We subsequently increase or decrease the carrying amount of the investment by our proportionate share of the net earnings or losses and other comprehensive income of the investee based on our percentage of common stock ownership during the respective reporting period. Payments to investees such as additional investments, loans, and expenses incurred on behalf of investees, as well as payments from investees such as dividends, distributions, and repayments of loans are recorded as adjustments to the carrying value of the investment. In the event that net losses of the investee reduce the carrying amount to zero, additional net losses may be recorded if we have other investment in the investee not accounted for under the equity method, have guaranteed obligations of the investee, or we are otherwise committed to provide further financial support for the investee.

We account for investments at fair value when we do not have significant influence over the investee. In the absence of readily determinable fair value, we measure the investment at cost less impairment plus or minus observable price changes, if any. We recognize income for any dividends declared from the distribution of the investee's earnings.

As of December 31, 2020, we had an equity method and equity security investments in PellePharm. The equity security investments in PellePharm were without a readily determinable fair value and were carried at cost less impairment plus or minus observable price changes. PellePharm became a consolidated VIE in April 2021. As of December 31, 2020, we had an equity method investment in LianBio representing ordinary shares held by BridgeBio Pharma, LLC ("BBP LLC"). In November 2021, we no longer held significant influence over LianBio and therefore began accounting for the investment in LianBio under ASC 321, *Investments — Equity Securities*. Refer to Note 7 for further discussion on the PellePharm and LianBio investments, both of which were no longer accounted for as equity method investments as of December 31, 2021. We no longer have any equity method investments as of December 31, 2022 and 2021.

Under the equity method of accounting, our investments are reviewed for indicators of impairment at each reporting period and are written down to fair value if there is evidence of a loss in value that is other-than-temporary. Factors that may be indicative of an impairment include a series of operating losses of an investee, the absence of an ability to recover the carrying amount of the investment, the inability of the investee to sustain an earnings capacity and a current fair value of an investment that is less than its carrying amount. Indicators that a decline in value may be other-than-temporary include the length of time and the extent to which the estimated fair value or market value has been below the carrying value, the financial condition and the near-term prospects of the investee, the intent and our ability to retain our investment in the investee for a period of time sufficient to allow for any anticipated recovery in market value and general market conditions. The estimation of fair value and whether an other-than-temporary impairment has occurred requires the application of significant judgment and future results may vary from current assumptions. No impairment charge was recognized for the years ended December 31, 2021 and 2020 related to our equity method investments.

Concentration of Credit Risk and Other Risks and Uncertainties

Financial instruments that subject us to significant concentrations of credit risk consist primarily of cash, cash equivalents and restricted cash. Substantially all of our cash, cash equivalents and restricted cash are held in financial institutions in the United States. Amounts on deposit may at times exceed federally insured limits. Management believes that the financial institutions are financially sound and, accordingly, minimal credit risk exists with respect to the financial institutions.

We are subject to certain risks and uncertainties and we believe that changes in any of the following areas could have a material adverse effect on future financial position or results of operations: ability to obtain future financing, regulatory approval and market acceptance of, and reimbursement for, product candidates, performance of third-party contract research organizations and manufacturers upon which we rely, development of sales channels, protection of our intellectual property, litigation or claims against us based on intellectual property, patent, product, regulatory, clinical or other factors, and our ability to attract and retain employees necessary to support our growth.

We are dependent on third-party manufacturers to supply products for research and development activities in our programs. In particular, we rely and expects to continue to rely on a small number of manufacturers to supply us with our requirements for the active pharmaceutical ingredients and formulated drugs related to these programs. These programs could be adversely affected by a significant interruption in the supply of active pharmaceutical ingredients and formulated drugs.

In March 2020, the World Health Organization declared the outbreak of SARS-CoV-2, the novel strain of coronavirus that causes Coronavirus disease 19, or COVID-19, a global pandemic. Since then, healthcare providers and hospitals have focused significant amounts of resources on fighting the virus and its variants, and we have experienced delays in or temporary suspension of the enrollment of patients in our subsidiaries' ongoing clinical trials. Additionally, we may experience delays in certain ongoing key program activities, including commencement of planned clinical trials, as well as non-clinical experiments and Investigational New Drug Application-enabling good laboratory practice toxicology studies. The exact timing of delays and their overall impact on our business are currently unknown and we are monitoring the ongoing COVID-19 pandemic as it continues to evolve. While certain measures have been relaxed in certain parts of the world as increasing numbers of people have received COVID-19 vaccines, others have remained in place with some areas continuing to experience renewed outbreaks and surges in infection rates. The extent to which such measures are removed or new measures are put in place will depend upon how the pandemic evolves, as well as the distribution of available vaccines, the rates at which they are administered and the emergence of new variants of the virus. We are continuing to actively monitor the situation and may take further precautionary and preemptive actions as may be required by federal, state, or local authorities or that we determine are in the best interests of public health and safety and that of our patient community, employees, partners, suppliers, and stockholders. We cannot predict the effects that such actions, or the impact of COVID-19 on global business operations and economic conditions, may have on our business or strategy, including the effects on our ongoing and planned clinical development activities and prospects or on our financial and operating results.

Use of Estimates

The preparation of consolidated financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets, liabilities, and disclosure of contingent liabilities at the date of the consolidated financial statements, and the reported amounts of expenses during the reporting period. Significant estimates and assumptions made in the accompanying consolidated financial statements include, but are not limited to:

- accruals for research and development activities and contingent clinical, development, regulatory, and sales-based milestone payments in our in-licensing agreements and asset acquisitions,
- accruals for performance-based milestone compensation arrangements,
- determining and allocating the transaction price to performance obligations for transactions accounted for under ASC 606, *Revenue from Contracts with Customers*,
- the expected recoverability and estimated useful lives of our long-lived assets, and
- additional charges as a result of, or that are associated with, any restructuring initiative as well as impairment and related charges.

We base our estimates on historical experience and on various other assumptions that are believed to be reasonable. Actual results may differ from those estimates or assumptions.

Cash, Cash Equivalents and Marketable Securities

We consider all highly liquid investments purchased with original maturities of 90 days or less from the purchase date to be cash equivalents. Cash equivalents consist primarily of amounts invested in money market instruments, such as money market funds and repurchase agreements collateralized with securities issued by the U.S. government or its agencies.

Our marketable securities consist of high investment grade fixed income securities that are primarily invested in commercial paper, corporate bonds, and U.S. government securities. We classify our marketable securities as available-for-sale securities and report them at fair value in cash equivalents or marketable securities on the consolidated balance sheets with related unrealized gains and losses included as a component of stockholders' deficit. We classify our marketable securities as either short-term or long-term based on each instrument's underlying contractual maturity date. The amortized cost of debt securities is adjusted for amortization of premiums and accretion of discounts to maturity which is included in interest income on the consolidated statements of operations. Realized gains and losses and declines in value judged to be other-than-temporary, if any, on available-for-sale securities are included in "Other income (expense), net". The cost of securities sold is based on the specific identification method. Interest and dividends on securities classified as available-for-sale are included in interest income.

Our cash, cash equivalents and marketable securities are exposed to credit risk in the event of default by the third parties that hold or issue such assets. Our cash, cash equivalents and marketable securities are held by financial institutions that management believes are of high credit quality. Our investment policy limits investments to fixed income securities denominated and payable in U.S. dollars such as corporate bonds, corporate commercial paper, U.S. government obligations, and money market funds, and places restrictions on maturities and concentrations by type and issuer.

The following table provides a reconciliation of cash, cash equivalents and restricted cash reported within the consolidated balance sheets that sum to the total of the amounts shown in the consolidated statements of cash flows:

	December 31,		
	2022	2021	2020
		(in thousands)	
Cash and cash equivalents	$ 376,689	$ 393,772	$ 356,082
Restricted cash	37,930	177	139
Restricted cash, non-current — included in "Other assets"	2,265	2,416	2,458
Total cash, cash equivalents and restricted cash shown in the consolidated statements of cash flows	$ 416,884	$ 396,365	$ 358,679

Restricted Cash

Restricted cash primarily represents funds in a controlled account that was established in connection with the Second Amendment of the Company's Loan and Security Agreement that is described in Note 10. The use of such non-interest-bearing cash is restricted per the terms of the underlying amended loan agreement and is to be used solely for certain research and development expenses directly attributable to the performance of obligations associated with the Navire-BMS License Agreement, which is further described in Note 11. As of December 31, 2022, restricted cash related to this agreement was $37.8 million, which is presented as part of "Restricted cash" on the consolidated balance sheets.

Additionally, under certain lease agreements and letters of credit, we have pledged cash and cash equivalents as collateral. As of December 31, 2022, restricted cash related to such agreements was $0.1 million and $2.3 million, which is presented as part of "Restricted cash" and "Other assets", respectively, on the consolidated balance sheets. As of December 31, 2021, restricted cash related to such agreements was $0.2 million and $2.4 million, which is presented as part of "Restricted Cash" and "Other Assets", respectively, on the consolidated balance sheets.

Investment in Equity Securities

We have investment in equity securities of public companies starting in 2021. We measure the fair value of our investment in equity securities at each reporting period in accordance with ASC 321, *Investments - Equity Securities*. Changes in fair value resulting from observable price changes are included in "Other income (expense), net" in our consolidated statements of operations. Upon sale of an equity security, any realized gain or loss is recognized in our consolidated statements of operations. We generally classify our investment in equity securities as a noncurrent asset. We classify our investment in equity securities as a current asset if we intend to liquidate these shares to fund current operations, should the need arise.

Fair Value Measurements

Assets and liabilities recorded at fair value on a recurring basis in the consolidated balance sheets are categorized based upon the level of judgment associated with the inputs used to measure their fair values. Fair value is defined as the exchange price that would be received for an asset or an exit price that would be paid to transfer a liability in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. Valuation techniques used to measure fair value must maximize the use of observable inputs and minimize the use of unobservable inputs. The authoritative guidance on fair value measurements establishes a three-tier fair value hierarchy for disclosure of fair value measurements as follows:

Level 1 — Observable inputs such as unadjusted, quoted prices in active markets for identical assets or liabilities at the measurement date.

Level 2 — Inputs (other than quoted prices included in Level 1) are either directly or indirectly observable for the asset or liability. These include quoted prices for similar assets or liabilities in active markets and quoted prices for identical or similar assets or liabilities in markets that are not active; and

Level 3 — Unobservable inputs that are supported by little or no market activity and that are significant to the fair value of the assets or liabilities.

To the extent that the valuation is based on models or inputs that are less observable or unobservable in the market, the determination of fair value requires more judgment. Accordingly, the degree of judgment we exercise in determining fair value is greatest for instruments categorized in Level 3. A financial instrument's level within the fair value hierarchy is based on the lowest level of any input that is significant to the fair value measurement.

The carrying amounts reflected in the accompanying consolidated balance sheets for cash and cash equivalents, restricted cash, receivable from licensing and collaboration agreements, prepaid expenses and other current assets, accounts payable, and accrued expenses approximate their fair values, due to their short-term nature.

Property and Equipment, net

Property and equipment are stated at cost, net of accumulated depreciation and amortization. Depreciation and amortization of property and equipment are calculated using the straight-line method over the estimated useful lives of the respective assets. Maintenance and repairs that do not improve or extend the life of the assets are expensed when incurred. Upon sale or retirement of assets, the cost and accumulated depreciation and amortization are removed from the consolidated balance sheet and any resulting gain or loss is reflected in the consolidated statement of operations in the period realized.

The estimated useful lives of our property and equipment are as follows:

Furniture and office equipment	3 - 5 years
Laboratory and machinery equipment	5 - 15 years
Leasehold improvements	Shorter of remaining lease term or estimated useful life of the related asset

Depreciation and amortization expense of property and equipment was $4.1 million and $3.3 million for the years ended December 31, 2022 and 2021, respectively. Depreciation and amortization expense was not material for the year ended December 31, 2020.

Leases

Our lease portfolio includes leases for our corporate headquarters, office spaces, and laboratory facilities. We determine if an arrangement is a lease at the inception of the contract. The asset component of our operating leases is recorded as “Operating lease right-of-use assets”, and the liability component is recorded as “Operating lease liabilities, current portion” and “Operating lease liabilities, net of current portion” in our consolidated balance sheets. The asset component of our finance leases is included in “Property and equipment, net”, and current and noncurrent finance lease liabilities are presented as part of “Other accrued liabilities” and “Other long-term liabilities”, respectively, in our consolidated balance sheets. Assets under finance leases are depreciated in a manner similar to other property and equipment.

Right-of-use assets and lease liabilities are recognized based on the present value of lease payments over the lease term at the lease commencement date. The present value of lease payments is determined by using the interest rate implicit in the lease, if that rate is readily determinable; otherwise, we use an incremental borrowing rate based on the information available at lease commencement date in determining the present value of lease payments. Right-of-use assets are adjusted for lease incentive amounts expected to be received. On the lease commencement date, we estimate and include in our lease payments any lease incentive amounts based on future events when (1) the events are within our control and (2) the event triggering the right to receive the incentive is deemed reasonably certain to occur. If the lease incentive received is greater or less than the amount recognized at lease commencement, we recognize the difference as an adjustment to right-of-use asset and/or lease liability, as applicable.

Right-of-use assets and lease liabilities are remeasured upon certain modifications to leases using the present value of remaining lease payments and estimated incremental borrowing rate upon lease modification. Operating lease cost is recognized on a straight-line basis over the lease term, and includes amounts related to short-term leases. For finance leases, we record interest expense on the lease liability in addition to amortizing the right-of-use asset, which is generally straight-line, over the shorter of the lease term or the useful life of the right-of-use asset. We recognize variable lease payments as operating expenses in the period in which the obligation for those payments is incurred. Variable lease payments primarily include common area maintenance, utilities, real estate taxes, insurance, and other operating costs that are passed on from the lessor in proportion to the space we lease.

Asset Acquisitions

We measure and recognize asset acquisitions that are not deemed to be business combinations based on the cost to acquire the assets, which includes transaction costs. Goodwill is not recognized in asset acquisitions. In an asset acquisition, the cost allocated to acquire in-process research and development, or IPR&D, with no alternative future use is charged to research and development expense at the acquisition date.

Impairment of Long-Lived Assets

Long-lived assets are reviewed for impairment annually or whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable. Recoverability is measured by comparison of the carrying amount of an asset group to the future net undiscounted cash flows that the assets are expected to generate. If the carrying amount of an asset group exceeds its estimated future cash flows, an impairment charge is recognized in the amount by which the carrying amount of the asset group exceeds the fair value of the asset group. Refer to Note 14 for impairment of certain long-lived assets recognized for the year ended December 31, 2022.

Segments

We are a single operating and reportable segment, which is in the business of identifying and advancing transformative medicines to treat patients. We operate in one segment because our business offerings have similar economics and other characteristics, including the nature of products and manufacturing processes, types of customers, distribution methods, and regulatory environment. We are comprehensively managed as one business segment by the Chief Operating Decision Maker, which is our Chief Executive Officer.

Total revenues, which are mainly from license and collaborative arrangements are attributed to regions based on the headquarters of the partner.

- For the year ended December 31, 2022, approximately 98.2% of our total revenue is from Bristol-Myers Squibb Company, or BMS with headquarters located in New York, United States.
- For the year ended December 31, 2021, approximately 80% and 13% of our total revenue is from Helsinn Healthcare S.A., or HHC, with headquarters located in Switzerland and from LianBio with headquarters located in Shanghai, China, respectively.
- For the year ended December 31, 2020, approximately 97% of our total revenue is from LianBio with headquarters located in Shanghai, China.

As of December 31, 2022, and 2021 our capitalized property and equipment located in the United States and Canada is approximately 73% and 27%, and 85% and 15%, respectively.

Capped Call Transactions

In January 2021 and March 2020, in connection with the issuance of the 2029 Notes and the 2027 Notes, respectively, (see Note 10), BridgeBio entered into certain capped call transactions, or the Capped Call Transactions. The Capped Call Transactions are generally expected to reduce the potential dilution to the holders of BridgeBio's common stock upon any conversion of the Notes and/or offset any cash payments BridgeBio is required to make in excess of the principal amount of converted Notes, with such reduction and/or offset subject to a cap based on the cap price (see Note 10). The capped calls meet the conditions outlined in ASC 815-40, *Derivatives and Hedging*, to be classified in stockholders' equity as a reduction to additional paid-in capital and are not subsequently remeasured as long as the conditions for equity classification continue to be met.

Debt Issuance Costs

Debt issuance costs are amortized to interest expense over the estimated life of the related debt based on the effective interest method. In accordance with ASC 835, *Interest*, we present debt issuance costs on the consolidated balance sheets as a direct deduction from the associated debt.

Treasury Stock

Repurchased treasury stock is recorded at cost, including any commissions and fees.

Collaborative Agreements

We enter into collaboration arrangements with partners, under which we may grant licenses to further develop, manufacture and commercialize our drug compounds and/or product candidates. We may also perform research, development, manufacturing, commercialization, and supply activities under our collaboration agreements. Consideration under these arrangements may include, upfront payments, development and regulatory milestones, expense reimbursements, royalties based on net sales of commercial products, and commercial sales milestone payments.

When we enter into collaboration agreements, we assess whether the arrangements fall within the scope of ASC 808, *Collaborative Arrangements,* based on whether the arrangements involve joint operating activities and whether both parties have active participation in the arrangement and are exposed to significant risks and rewards. To the extent that the arrangement falls within the scope of ASC 808, we assess whether the payments between us and our partner fall within the scope of other accounting literature. If we conclude that payments from the partner to us represent consideration from a customer, such as license fees, contract manufacturing, and research and development activities, we account for those payments within the scope of ASC 606. However, if we conclude that our partner is not a customer for certain activities and associated payments, such as for certain collaborative research, development, manufacturing, and commercial activities, we record such payments as a reduction of research and development expense or selling, general and administrative expense, based on where we present the underlying expense. Additionally, if we reimburse our collaboration partners for these activities, we record such reimbursements as research and development expense or selling, general and administrative expense, depending upon the nature of the underlying expense.

If our collaborative arrangement provides for the sharing of profits and losses with our partner for commercialization activities, the treatment of our share in the profit-sharing structure depends on who the selling party is. If we are the selling party and the deemed principal, we record our collaboration partner's share of profits as an addition to selling, general and administrative expenses and our collaboration partner's share of loss as a reduction in selling, general and administrative expenses. If our partner is the selling party and the deemed principal, we record our share of profits as collaboration revenue and our share of losses as an addition to selling, general and administrative expenses.

Revenue Recognition

For elements or transactions that we determine should be accounted for under ASC 606, we perform the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) we satisfy our performance obligation. We apply the five-step model to contracts when it is probable that we will collect the consideration to which we are entitled in exchange for the goods or services we transfer to the customer.

At inception of the arrangement, we assess the promised goods or services to identify the performance obligations within the contract. We then recognize as revenue the amount of the transaction price that is allocated to the respective performance obligation, on a relative standalone selling price basis, when (or as) the performance obligation is satisfied, either at a point in time or over time. If the performance obligation is satisfied over time, we recognize revenue based on the use of an input method. As part of the accounting for these arrangements, we develop assumptions that require judgment to determine the standalone selling price for each performance obligation identified in the contract. These key assumptions may include forecasted revenue or costs, development timelines, discount rates and probabilities of clinical and regulatory success.

License Fees: For arrangements that include a grant of a license to our intellectual property, we consider whether the license grant is distinct from the other performance obligations included in the arrangement. Generally, we would conclude that the license is distinct if the customer is able to benefit from the license with the resources available to it. For licenses that are distinct, we recognize revenues from nonrefundable, upfront license fees and other consideration allocated to the license when the license term has begun and we have provided all necessary information regarding the underlying intellectual property to the customer, which generally occurs at or near the inception of the arrangement. For licenses that are bundled with other promises, we determine whether the combined performance obligation is satisfied over time or at a point in time. If the combined performance obligation is satisfied over time, we use judgment in determining the appropriate method of measuring progress for purposes of recognizing revenue from the up-front license fees. We evaluate the measure of progress each reporting period and, if necessary, adjust the measure of performance and related revenue recognition.

Development and Regulatory Milestone Payments: At the inception of each arrangement that includes development and regulatory milestone payments, we evaluate whether the milestones are considered probable of being achieved and estimate the amount to be included in the transaction price using the most likely amount method. We generally include these milestone payments when they are achieved because there is considerable uncertainty in the research and development processes that trigger these payments under our agreements. Similarly, we include approval milestone payments in the transaction price once the product is approved by the applicable regulatory agency. At the end of each subsequent reporting period, we re-evaluate the probability of achieving such development and regulatory milestones and any related constraint, and if necessary, adjust our estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis.

Sales-based Milestone Payments and Royalties: For arrangements that include sales-based royalties, including milestone payments based on the volume of sales, we will determine whether the license is deemed to be the predominant item to which the royalties or sales-based milestones relate and if such is the case, we will recognize revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied).

Product supply services: Arrangements that include a promise for the future supply of drug product for either clinical development or commercial supply at the licensee’s discretion are generally considered as options. We will assess if these options provide a material right to the licensee and if so, they are accounted for as separate performance obligations and recognized when the future goods or services related to the option are provided or the option expires.

Research and Development Services: For arrangements that include research and development services, we will recognize revenue over time using an input method, representing the transfer of goods or services as we perform activities over the term of the agreement.

Receivables from Licensing and Collaboration Agreements

Receivables from licensing and collaboration agreements represent valid claims against our partners, customers, biopharmaceutical companies including unbilled receivables and royalty payments due from third parties for licensing the Company’s technologies. Unbilled receivables include balances due from our biopharmaceutical customers related to development services and transition-related receivables that are recognized upon incurrence of the costs for the partnered programs but prior to the achievement of contractual billing rights. As of December 31, 2022, and 2021, the Company had unbilled receivables of $16.8 million and $6.3 million, respectively. As of December 31, 2022 and 2021, respectively, 97.5% and 94.3% of total unbilled receivables related to one partner. Total receivables from licensing and collaboration agreements as of December 31, 2022 and 2021, respectively, are presented as "Receivable from licensing and collaboration agreements" in our consolidated balance sheets.

The Company evaluates the collectability of its receivable from licensing and collaboration agreements based on historical collection trends, the financial condition of payment partners, customers, and biopharmaceutical companies, and external market factors and provides for an allowance for potential credit losses based on management’s best estimate of the amount of probable credit losses. As of December 31, 2022 and 2021, the Company did not have an allowance for credit losses.

Research and Development Expenses

Research and development costs are expensed as incurred. Research and development expenses consist of salaries, benefits and other personnel related costs including stock-based compensation expense, laboratory supplies, preclinical studies, clinical trials and related clinical manufacturing costs, costs related to manufacturing preparations, fees paid to other entities to conduct certain research and development activities on our behalf, and allocated facility and other related costs. Non-refundable advance payments for goods or services that will be used or rendered for future research and development activities are deferred and capitalized as prepaid expenses until the related goods are delivered or services are performed.

Accrued Research and Development Liabilities

We record accruals for estimated costs of research and development activities conducted by third-party service providers, which include the conduct of preclinical studies, clinical trials, and contract manufacturing activities. We record the estimated costs of research and development activities based upon the estimated amount of services provided but not yet invoiced, and include these costs in accrued research and development liabilities in the consolidated balance sheets and within research and development expense in the consolidated statements of operations. These costs are a significant component of our research and development expenses.

Examples of estimated research and development expenses that we accrue include:

- fees paid to CROs in connection with preclinical and toxicology studies and clinical trials;
- fees paid to investigative sites in connection with clinical trials;
- fees paid to CMOs in connection with the production of product and clinical trial materials; and
- professional service fees for consulting and related services.

We base our expense accruals related to clinical trials on our estimates of the services received and efforts expended pursuant to contracts with multiple research institutions and CROs that conduct and manage clinical trials on our behalf. The financial terms of these agreements vary from contract to contract and may result in uneven payment flows. Payments under some of these contracts depend on factors, such as the successful enrollment of patients and the completion of clinical trial milestones. Our service providers generally invoice us monthly in arrears for services performed. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If we do not identify costs that we have begun to incur or if we underestimate or overestimate the level of services performed or the costs of these services, our actual expenses could differ from our estimates. We record advance payments to service providers as prepaid assets.

We record accruals for the estimated costs of our contract manufacturing activities performed by third parties. The financial terms of these agreements are subject to negotiation, vary from contract to contract, and may result in uneven payment flows to our vendors. Payments under the contracts include upfront payments and milestone payments, which depend on factors such as the achievement of the completion of certain stages of the manufacturing process. For purposes of recognizing expense, we assess whether we consider the production process sufficiently defined to be considered the delivery of a good or the delivery of a service, where processes and yields are developing and less certain. If we consider the process to be the delivery of a good, we recognize expense when the drug product is delivered, or we otherwise bear risk of loss. If we consider the process to be the delivery of a service, we recognize expense based on our best estimates of the contract manufacturer’s progress towards completion of the stages in the contract. We base our estimates on the best information available at the time. However, additional information may become available to us which may allow us to make a more accurate estimate in future periods. In this event, we may be required to record adjustments to research and development expenses in future periods when the actual level of activity becomes more certain. Any increases or decreases in cost are generally considered to be changes in estimates and will be reflected in research and development expenses in the period identified.

Milestone and Royalty Payments Under Asset Acquisitions, In-licensing and Other Agreements

Under our asset acquisitions, in-licensing, and other agreements, we could be required to pay development, regulatory, and sales-based milestone payments if certain substantive milestones are met. We generally expense development milestones as incurred. For regulatory or sales-based milestones that are associated with an approved asset, we capitalize the milestone payments related to the asset purchase as a finite-lived intangible asset provided that the milestone payment is recoverable based on our estimated projected cash flows and if the asset has alternative future use. Such intangible asset is amortized over its estimated useful life on a straight-line basis, beginning on the date the asset is acquired, which would generally be the regulatory approval date. We assess the carrying value of our finite-lived intangible assets for impairment whenever events or changes in circumstances indicate that the carrying value may not be fully recoverable. Recoverability of finite-lived intangible assets is measured by comparison of the carrying value of the asset to the future undiscounted cash flows the asset is expected to generate.

We could also be required to pay royalties based on actual net sales under in-licensing agreements and asset acquisitions. Such royalties are expensed in the period of sale of the product.

Sales of Nonfinancial Assets

We generally account for sales of nonfinancial assets that are outside the scope of our ordinary activities under ASC 610-20, *Other Income - Gains and Losses from the Derecognition of Nonfinancial Assets*. Pursuant to ASC 610-20, we apply the guidance in ASC 606 to determine if a contract exists, identify the distinct nonfinancial assets, and determine when control transfers and, therefore, when to derecognize the nonfinancial asset. Additionally, we apply the measurement principles of ASC 606 to determine the amount of consideration, if any, to include in the calculation of the gain or loss for the sale of the nonfinancial asset.

Restructuring, Impairment and Related Charges

Long-lived assets are reviewed for impairment annually or whenever events or changes in circumstances, including restructuring and exit activities, indicate that the carrying amount of an asset may not be recoverable. Recoverability is measured by comparison of the carrying amount of an asset group to the future net undiscounted cash flows that the assets are expected to generate. If the carrying amount of an asset group exceeds its estimated future cash flows, an impairment charge is recognized in the amount by which the carrying amount of the asset group exceeds the fair value of the asset group.

Costs related to contracts without future benefit or contract termination costs are recognized at the earlier of the contract termination or the cease-use dates. Employee severance costs are generally recognized when payments are probable and amounts are reasonably estimable. Other winding down and exit-related costs are recognized as incurred.

Stock-Based Compensation

Stock-based compensation arrangements include stock option grants, restricted stock awards, or RSA, and restricted stock units, or RSU awards under our equity incentive plans, as well as shares issued under our Employee Stock Purchase Plan, or ESPP, through which employees may purchase our common stock at a discount to the market price.

We use the Black-Scholes option pricing model to estimate the fair value of options granted under our equity incentive plans and rights to acquire shares granted under our ESPP. The Black-Scholes option valuation model requires the use of assumptions, including the expected term of the award and the expected share price volatility. We use the “simplified” method to estimate the expected option term.

Stock-based compensation is measured at the grant date for all stock-based awards made to employees and non-employees based on the fair value of the awards. Compensation expense for purchases under the ESPP is recognized based on the fair value of the award on the date of offering. Stock-based compensation is recognized as expense on a straight-line basis over the requisite service period, which is generally the vesting period.

The estimated fair value of equity awards that contain performance conditions is expensed using an accelerated method over the term of the award once we have determined that it is probable that performance milestones will be achieved. Compensation expense for equity-classified awards that contain performance conditions is measured based on the grant date fair value of the award. Compensation expense for liability-classified awards that contain performance conditions is initially measured based on the grant date fair value of the award and is remeasured at fair value at each reporting date until the date of settlement. Compensation expense is recorded over the requisite service period based on management’s best estimate as to whether it is probable that the shares awarded are expected to vest. We assess the probability of the performance milestones being met on a continuous basis.

We have elected to recognize the actual forfeitures by reducing the stock-based compensation in the same period as the forfeitures occur.

Stock-based compensation is generally recorded in research and development expense, and selling, general and administrative expense based on the function of the applicable employee and non-employee.

Accrued Milestone Compensation Arrangements

We have performance-based milestone compensation arrangements with certain employees and consultants, whose vesting is contingent upon meeting various regulatory and development milestones, with fixed monetary amounts known at inception that can be settled in the form of (1) cash, (2) equity of BridgeBio, or (3) cash or equity of BridgeBio at our sole election, upon achievement of each contingent milestone. For arrangements that involve settlement by cash or equity of BridgeBio at our sole election, we will classify the milestone compensation arrangements as liability-classified awards when it is probable of achievement because of the possible fixed monetary amounts settlement outcomes. The arrangements would also result in settlement with a variable number of shares based on the then-current stock price at achievement date of each contingent milestone should we elect to settle in equity.

We record accruals for the compensation expense arising from each development milestone when the specific contingent development milestone is probable of achievement and such accruals are measured at each reporting period. We estimate the probability of achieving such milestones based on the progression and expected outcome of the related clinical programs. We base our estimates on the best available information at that time. However, additional information may become available to us which may allow us to make a more accurate estimate in future periods. In this event, we may be required to record adjustments to milestone compensation expenses in future periods. Any increases or decreases in such expenses are generally considered to be changes in estimates and will be reflected in the period identified.

Income Taxes

Income taxes are accounted for under the asset and liability method. Deferred tax assets and liabilities are recognized for the future tax consequences attributable to differences between the financial statement carrying amounts of existing assets and liabilities and their respective tax base and net operating loss and tax credit carryforwards. Deferred tax assets and liabilities are determined based upon the difference between the consolidated financial statement carrying amounts and the tax basis of assets and liabilities and are measured using the enacted tax rate expected to apply to taxable income in the years in which the differences are expected to be reversed. Deferred tax assets are reduced by a valuation allowance if it is more likely than not that some portion or all of the deferred tax asset will not be realized.

For U.S. federal income tax purposes, we are required to file a consolidated U.S. federal income tax return for the consolidated entities which meet the requirements as prescribed by the consolidated regulations. Those entities that do not meet the threshold to be included in the consolidated filing continue to file separate U.S. federal income tax returns. We are required to assess stand-alone valuation allowances separately in each entity even though we consolidate their financial results in the consolidated financial statements. We continue to file combined state tax returns in most jurisdictions. As a result, we continue to assess the state portion of valuation allowance for those jurisdictions on a consolidated basis. The Company also operates in various foreign jurisdictions and assesses stand-alone valuation allowances separately in each entity operating overseas.

We evaluate our deferred tax assets regularly to determine whether adjustments to the valuation allowance are appropriate due to changes in facts or circumstances, such as changes in expected future pre-tax earnings, tax law, interactions with taxing authorities and developments in case law. In making this evaluation, we rely on our recent history of pre-tax earnings. Our material assumptions are our forecasts of future pre-tax earnings and the nature and timing of future deductions and income represented by the deferred tax assets and liabilities, all of which involve the exercise of significant judgment. Although we believe our estimates are reasonable, we are required to use significant judgment in determining the appropriate amount of valuation allowance recorded against deferred tax assets.

We recognize uncertain income tax positions at the largest amount that is more likely than not to be sustained upon audit by the relevant taxing authority. Changes in recognition or measurement are reflected in the period in which judgment occurs. Our policy is to recognize interest and penalties related to the underpayment of income taxes as a component of the provision for income taxes. To date, there have been no interest or penalties recorded in relation to unrecognized tax benefits.

LEO Call Option Liability

We accounted for the LEO Call Option as a current liability as we had the obligation to sell our PellePharm shares to LEO at a pre-determined price if the option is exercised. The LEO Call Option liability was recorded at fair value upon execution of the LEO Agreement. The LEO Call Option liability was subject to remeasurement to fair value at each balance sheet date until the LEO Call Option was either exercised, terminated or it expired as it did not qualify for equity classification. Any change in the fair value of the LEO Call Option liability was recognized as a component of “Other income (expense), net” in the consolidated statements of operations. The LEO Call Option was terminated by LEO in 2021 and, therefore, no longer outstanding as of December 31, 2022. Refer to Notes 3 and 7 for further discussion.

Net Loss per Share Attributable to Common Stockholders of BridgeBio

Basic net loss per share attributable to common stockholders of BridgeBio is calculated by dividing the net loss attributable to common stockholders of BridgeBio by the weighted-average number of shares of BridgeBio’s common stock outstanding for the period, without consideration for potential dilutive shares of common stock, such as stock options, unvested restricted stock units and awards and performance-based milestone compensation awards, shares issuable under the employee stock purchase plan and assumed conversion of our 2029 and 2027 Notes. The common stock equivalents of performance-based milestone compensation arrangements are included as potentially dilutive shares only if the performance condition has been met as of the end of the reporting period. Shares of common stock subject to repurchase are excluded from the weighted-average shares. Since we were in a loss position for all periods presented, basic net loss per share attributable to common stockholders of BridgeBio is the same as diluted net loss per share attributable to common stockholders of BridgeBio since the effects of potentially dilutive securities are antidilutive.

Recently Adopted Accounting Pronouncements

There have been no significant changes in recently adopted or issued accounting pronouncements from those disclosed in the section titled “Financial Statements and Supplementary Data” included in our Annual Report on Form 10-K for the year ended December 31, 2021, as filed with the SEC. We have reviewed all recently issued accounting pronouncements and have determined that such standards that are not yet effective will not have a material impact on our financial statements or do not otherwise apply to our operations.

3. Fair Value Measurements

The following table presents information about our financial assets and liabilities that are measured at fair value on a recurring basis and indicates the fair value hierarchy of the valuation:

	December 31, 2022			
	Total	Level 1	Level 2	Level 3
	(in thousands)			
Assets				
Cash equivalents:				
Money market funds	$ 202,250	$ 202,250	$ —	$ —
Commercial paper	159,758	—	159,758	—
Total cash equivalents	362,008	202,250	159,758	—
Marketable securities:				
Commercial paper	51,580	—	51,580	—
Total marketable securities	51,580	—	51,580	—
Investment in equity securities	43,653	43,653	—	—
LianBio Warrant	570	570	—	—
Total financial assets	$ 457,811	$ 246,473	$ 211,338	$ —
Liability				
Embedded derivative	$ 1,201	$ —	$ —	$ 1,201

	December 31, 2021			
	Total	Level 1	Level 2	Level 3
	(in thousands)			
Assets				
Cash equivalents:				
Money market funds	$ 176,115	$ 176,115	$ —	$ —
Commercial paper	56,986	—	56,986	—
Total cash equivalents	233,101	176,115	56,986	—
Marketable securities:				
U.S. treasury notes	76,472	—	76,472	—
Commercial paper	167,737	—	167,737	—
Corporate debt securities	122,490	—	122,490	—
Supranational debt securities	27,044	—	27,044	—
Total marketable securities	393,743	—	393,743	—
Investment in equity securities	49,148	49,148	—	—
LianBio Warrant	2,141	2,141	—	—
Total financial assets	$ 678,133	$ 227,404	$ 450,729	$ —
Liability				
Embedded derivative	$ 1,171	$ —	$ —	$ 1,171

There were no transfers between Level 1, Level 2 or Level 3 during the periods presented.

There are uncertainties on the fair value measurement of the instruments classified under Level 3 due to the use of unobservable inputs and interrelationships between these unobservable inputs, which could result in higher or lower fair value measurements.

Marketable Securities

The fair value of our marketable securities classified within Level 2 is based upon observable inputs that may include benchmark yields, reported trades, broker/dealer quotes, issuer spreads, two-sided markets, benchmark securities, bids, offers, and reference data including market research publications.

Investment in Equity Securities

We have investment in equity securities of publicly held companies, which are actively traded with quoted prices that are readily available, and we do not have restrictions on our ability to sell these securities. Therefore, these are classified within Level 1. Our investment in equity securities had an aggregate fair value of $35.5 million and $18.3 million as of December 31, 2022 and 2021, respectively. We had no investment in equity securities of publicly held companies as of December 31, 2020.

As of December 31, 2022, and 2021, we have an investment in LianBio whose fair value amounted to $8.2 million and $30.8 million, respectively. This investment was originally accounted for under the equity method until it was converted into an investment in equity securities that is accounted for under ASC 321 upon completion of LianBio's initial public offering, or IPO, in November 2021 (see Note 7). The LianBio shares were subject to a lock-up agreement, which restricted our ability to sell the securities through April 2022.

Total realized and unrealized gains and losses associated with investment in equity securities for the periods presented consisted of the following:

	Year Ended December 31,	
	2022	2021
	(in thousands)	
Gain on conversion from equity method investment to investment in equity securities	$ —	$ 68,538
Net realized gains recognized on investment in equity securities sold	3,731	2,206
Net unrealized losses recognized on investment in equity securities held as of the end of the period	(11,953)	(40,830)
Total net (losses) gains included in "Other income (expense), net"	$ (8,222)	$ 29,914

LianBio Warrant

As of December 31, 2022, and 2021, our subsidiary, QED Therapeutics, Inc, or QED, held a warrant which entitles QED to purchase shares of LianBio, or the LianBio Warrant, see Note 7. We classify the LianBio Warrant, which pertains to an equity security of a publicly held company, within Level 1 as the fair value of this equity security is derived from observable inputs such as quoted prices in an active market.

LEO Call Option Liability

As of December 31, 2022 and 2021, we no longer recognized the LEO Call Option that we previously carried as a liability in our consolidated balance sheets. In November 2018, LEO Pharma, or LEO, was granted an exclusive, irrevocable option to acquire our subsidiary, PellePharm, Inc, or PellePharm. The LEO Call Option was exercisable by LEO on or before the occurrence of certain events relating to PellePharm's clinical development programs and no later than July 30, 2021. We accounted for the LEO Call Option as a current liability because we were obligated to sell our shares in PellePharm to LEO at a pre-determined price if the option were to be exercised. We remeasured the LEO Call Option to fair value at each subsequent balance sheet date, using unobservable inputs that were classified as Level 3 inputs, until the LEO Call Option either was exercised, terminated or had expired. On March 30, 2021, LEO provided a notice of termination of the LEO Call Option effective April 15, 2021. As a result and based on the facts and circumstances that existed as of March 31, 2021, we evaluated that the likelihood of LEO exercising said option was remote and we remeasured the LEO Call Option liability to zero as of March 31, 2021. We recognized a gain on remeasurement of the LEO Call Option liability of $5.6 million recorded in "Other income (expense), net" for the year ended December 31, 2021.

Notes

The fair value of our 2029 Notes and our 2027 Notes, or, collectively, the Notes, see Note 10, which differ from their respective carrying values, are determined by prices for the Notes observed in market trading. The market for trading of the Notes is not considered to be an active market and therefore the estimate of fair value is based on Level 2 inputs. As of December 31, 2022, the estimated fair value of our 2029 Notes and 2027 Notes, which have aggregate face values of $747.5 million and $550.0 million, respectively, were $314.0 million and $218.6 million, respectively, based on their market prices on the last trading day for the period. As of December 31, 2021, the estimated fair value of our 2029 Notes and 2027 Notes, were $444.8 million and $407.1 million, respectively, based on their market prices on the last trading day for the period.

Term Loan

The fair value of our outstanding term loan as of December 31, 2022 and 2021 (see Note 10) is estimated using the net present value of the payments, discounted at an interest rate that is consistent with a market interest rate, which is a Level 2 input. The estimated fair value of our outstanding term loan as of December 31, 2022 was $377.2 million. The estimated fair value of our outstanding term loan as of December 31, 2021 approximated the carrying amount as the term loan was issued close to the reporting period.

4. Cash Equivalents and Marketable Securities

We invest in certain U.S. government money market funds classified as cash equivalents. The marketable securities consist of high investment grade fixed income securities that are primarily invested in commercial paper, corporate bonds, and U.S. government securities.

Cash equivalents and marketable securities classified as available-for-sale consisted of the following:

	December 31, 2022			
	Amortized Cost Basis	Unrealized Gains	Unrealized Losses	Estimated Fair Value
	(in thousands)			
Cash equivalents:				
Money market funds	$ 202,250	$ —	$ —	$ 202,250
Commercial paper	159,812	—	(54)	159,758
Total cash equivalents	362,062	—	(54)	362,008
Marketable securities:				
Commercial paper	51,854	—	(274)	51,580
Total marketable securities	51,854	—	(274)	51,580
Total cash equivalents and marketable securities	$ 413,916	$ —	$ (328)	$ 413,588

	December 31, 2021			
	Amortized Cost Basis	Unrealized Gains	Unrealized Losses	Fair Value
	(in thousands)			
Cash equivalents:				
Money market funds	$ 176,115	$ —	$ —	$ 176,115
Commercial paper	56,988		(2)	56,986
Total cash equivalents	233,103	0	(2)	233,101
Marketable securities:				
U.S. treasury notes	76,518	—	(46)	76,472
Commercial paper	167,761	2	(26)	167,737
Corporate debt securities	122,548	—	(58)	122,490
Supranational debt securities	27,046	—	(2)	27,044
Total marketable securities	393,873	2	(132)	393,743
Total cash equivalents and marketable securities	$ 626,976	$ 2	$ (134)	$ 626,844

There have been no significant realized gains or losses on available-for-sale securities for the periods presented. As of December 31, 2022 and 2021, our marketable securities have average contractual maturities of approximately six months. We believe that we have the ability to realize the full value of all of these investments upon their respective maturities.

5. Eidos Therapeutics, Inc, or Eidos

From the date of BridgeBio's initial investment until June 22, 2018, the Eidos IPO closing date, Eidos was determined to be a VIE and BridgeBio consolidated Eidos as the primary beneficiary. Subsequent to the Eidos IPO, BridgeBio determined that Eidos was no longer a VIE due to Eidos having sufficient equity at risk to finance its activities without additional subordinated financial support. From June 22, 2018, through January 26, 2021, BridgeBio determined that it held greater than 50% of the voting shares of Eidos and there were no other parties with substantive participating, liquidation or kick-out rights. BridgeBio consolidated Eidos under the VOE model until January 26, 2021, the date on which the Merger Transactions (as defined below) were consummated.

On October 5, 2020, we entered into an Agreement and Plan of Merger, or the Merger Agreement, with Eidos, Globe Merger Sub I, Inc., or Merger Sub, and Globe Merger Sub II, Inc. (the two latter companies being our indirect wholly-owned subsidiaries), providing for, in a series of merger transactions, or the Merger Transactions, the acquisition by us of all of the outstanding shares of common stock of Eidos, or the Eidos Common Stock, other than shares of Eidos Common Stock that (i) were owned by Eidos as treasury stock, (ii) were owned by us and our subsidiaries and, in each case, not owned on behalf of third parties and (iii) were subject to an Eidos Restricted Share Award (as defined below). Under the Merger Agreement, the stockholders of Eidos had the right to receive, at their election, either 1.85 shares of our common stock or $73.26 in cash per Eidos share in the transaction, subject to proration as necessary to ensure that the aggregate amount of cash consideration was no greater than $175.0 million. In addition, immediately prior to the effective time of the merger of Merger Sub with and into Eidos, or the Effective Time, (i) each option to purchase Eidos Common Stock, or an Eidos Option were to be converted into an option, on the same terms and conditions applicable to such Eidos Option immediately prior to the Effective Time, to purchase a specified number of shares of BridgeBio common stock, calculated pursuant to the terms of the Merger Agreement, and (ii) each outstanding award of shares of Eidos Common Stock that was subject to forfeiture conditions (subject to certain exceptions), or, each, an Eidos Restricted Share Award was to be converted into an award, on the same terms and conditions applicable to such Eidos Restricted Share Award immediately prior to the Effective Time, covering a number of whole restricted shares of BridgeBio common stock, calculated pursuant to the terms of the Merger Agreement, with any fractional shares being paid out to the holder of such Eidos Restricted Share Award in cash (conversion of the Eidos Option and the Eidos Restricted Share Awards collectively referred to as the “Eidos Awards Exchange”).

On January 19, 2021, the stockholders of each of BridgeBio and Eidos voted to approve all proposals related to the Merger Transactions and on January 26, 2021, we closed and completed the Merger Transactions. The acquisition of the Eidos Common Stock was settled through an aggregate consideration of $1,651.6 million, which was comprised of cash payments of $21.3 million and the issuance of approximately 26,156,446 shares of our common stock, with a total fair value of $1,630.3 million. We accounted for the purchase of the outstanding Eidos Common Stock as acquisition of noncontrolling interest in accordance with ASC 810, *Consolidation*. Under ASC 810, the carrying amount of the Eidos noncontrolling interest was adjusted to reflect the change in our ownership interest, and the difference between the fair value of the consideration paid, and the amount by which the noncontrolling interest was adjusted was recognized in equity. Such difference recognized in equity amounted to $1,613.4 million and recorded as reduction in “Additional paid-in capital” for the year ended December 31, 2021. We continued to recognize the assets and liabilities of Eidos at their respective historical values as of the closing date of the Merger Transactions.

Through the closing of the Merger Transactions, we have incurred transaction costs aggregating $70.7 million that were recorded in “Additional paid-in capital” for the year ended December 31, 2021.

Upon closing and completion of the Merger Transactions with Eidos, Eidos became our wholly-owned subsidiary. Eidos’ common stock ceased to trade on The Nasdaq Global Select Market prior to the opening of business on January 26, 2021 and Eidos’ Certification and Notice of Termination of Registration under Section 12(g) of the Exchange Act was filed with the SEC on February 5, 2021.

6. Noncontrolling Interests

As of December 31, 2022, and 2021, we had both redeemable convertible noncontrolling interests and noncontrolling interests in consolidated partially-owned entities, for which BridgeBio is the primary beneficiary under the VIE model. These balances are reported as separate components outside stockholders’ deficit in “Redeemable convertible noncontrolling interests” and as part of stockholders’ deficit in “Noncontrolling interests” in the consolidated balance sheets.

We adjust the carrying value of noncontrolling interests to reflect the book value attributable to noncontrolling shareholders of consolidated partially-owned entities when there is a change in the ownership during the respective reporting period. For the years ended December 31, 2022, 2021, and 2020, such adjustments in the aggregate amounts of $(3.5) million, $(2.1) million and $12.0 million, respectively, are recorded to additional paid-in capital. All such adjustments are disclosed within the “Transfers from (to) noncontrolling interests” line item in the consolidated statements of redeemable convertible noncontrolling interests and stockholders’ equity (deficit).

7. Equity Method and Other Equity Investments

LianBio

In October 2019, BBP LLC entered into an exclusivity agreement with LianBio, pursuant to which BBP LLC received equity in LianBio representing a 10% ownership interest, valued at approximately $3.8 million at the time of the transaction and recognized as license revenue for the year ended December 31, 2019. The equity interest was issued in consideration for certain rights of first negotiation and rights of first offer granted by BBP LLC to LianBio with respect to specified transactions covering intellectual property rights owned or controlled by BBP LLC or its affiliates in certain territories outside the United States. The equity interest gave BBP LLC the right to appoint or remove one director to the board of directors of LianBio, and, therefore, can exercise significant influence over LianBio. As a result, we accounted for this investment under the equity method and LianBio was considered a related party.

The carrying value of our 10% ownership interest was reduced to zero as of December 31, 2019 after recognizing our equity share in the net losses of LianBio for the year ended December 31, 2019. As of December 31, 2020, our equity method investment in LianBio represented approximately 6% of LianBio's fully-diluted equity.

The carrying amount of the equity method investment in LianBio in the consolidated balance sheet as of December 31, 2020 represented our maximum loss exposure related to our investment in LianBio. There were no impairments related to the LianBio investment during the periods presented in which we applied the equity method.

On November 1, 2021, LianBio completed its IPO. Upon completion of the LianBio IPO, BBP LLC's ownership in LianBio was reduced to approximately 4.7% of LianBio's fully-diluted equity and, pursuant to the exclusivity agreement, BBP LLC's right to appoint or remove one director to the board of directors of LianBio was terminated. BBP LLC no longer exercises significant influence over LianBio; and, therefore, we started accounting for BBP LLC's equity interest in LianBio under ASC 321. LianBio is also no longer considered a related party. Consequently, we recognized a $68.5 million gain on conversion from equity method investment to investment in equity securities which is presented as part of "Other income (expense), net" in our consolidated statement of operations for the year ended December 31, 2021. For the years ended December 31, 2022 and 2021, we recorded $22.6 million and $37.7 million, respectively of unrealized loss for the ongoing mark-to-market adjustments of our investment, see Note 3.

Pursuant to a License Agreement entered into in October 2019 between QED and LianBio, or the QED-LianBio License Agreement (see Note 11), QED also received warrants which entitle QED to purchase 10% of the then-fully diluted shares of one of the subsidiaries of LianBio upon achievement of certain contingent development milestones. For the years ended December 31, 2020, certain contingent development milestones related to our ability to exercise the warrants to purchase shares in the LianBio subsidiary were achieved, and, as a result, we recognized changes in the fair value of the warrants of approximately $3.3 million in "Other income (expense), net" in our consolidated statements of operations for the year ended December 31, 2020. Changes in fair value of the warrants were not material for the years ended December 31, 2022 and 2021.

In October 2021, the warrants held by QED to purchase shares of one of the subsidiaries of LianBio were converted into the LianBio Warrant, which entitles QED to purchase 347,569 shares of LianBio. The LianBio Warrant is measured at fair value on a recurring basis, with changes in fair value recognized in our consolidated statements of operations as part of "Other income (expense), net". The LianBio Warrant, which is presented as part of "Other assets" in our consolidated balance sheets, had a fair value of $0.6 million and $2.1 million as of December 31, 2022 and 2021, respectively.

PellePharm

On November 19, 2018, PellePharm, Inc. entered into the LEO Agreement, pursuant to which LEO Pharma, or LEO was granted an exclusive, irrevocable option to acquire PellePharm. The LEO Call Option was exercisable by LEO on or before the occurrence of certain events relating to PellePharm's clinical development programs and no later than July 30, 2021. We accounted for the LEO Call Option as a current liability, or the LEO Call Option Liability, see Note 3 in our consolidated financial statements because BridgeBio was obligated to sell its shares in PellePharm to LEO at a pre-determined price if the option were to be exercised. We remeasured the LEO Call Option to fair value at each subsequent balance sheet date until the LEO Call Option either was exercised, terminated, or had expired.

Prior to the LEO Agreement, BridgeBio consolidated PellePharm under the VIE model. The date the LEO Agreement was entered into was determined to be a VIE reconsideration event. Based on our assessment, we had concluded that PellePharm remained a VIE after the reconsideration event as it did not have sufficient equity at risk to finance its activities without additional subordinated financial support. However, based on the then changes to PellePharm's governance structure and composition of the board of directors as a result of the LEO Agreement, BridgeBio was no longer the primary beneficiary as it no longer had the power over the key decisions that most significantly impact PellePharm's economic performance. Accordingly, BridgeBio deconsolidated PellePharm on November 19, 2018. After the deconsolidation in November 2018, PellePharm was considered a related party of BridgeBio.

Subsequent to the deconsolidation of PellePharm in 2018, we accounted for our retained common stock investment as an equity method investment and our retained preferred stock investment as a cost method investment. Upon adoption of Accounting Standards Update "ASU" 2016-01, *Financial Instruments – Overall (Subtopic 825-10): Recognition and Measurement of Financial Assets and Financial Liabilities* in 2019, we accounted for the investment in PellePharm preferred stock as an equity security without a readily determinable fair value. As of December 31, 2020, the aggregate carrying amount of our investments in PellePharm was zero. After the equity method investment was reduced to zero during the three months ended March 31, 2019, BridgeBio subsequently recorded its percentage of net losses consistent with its preferred stock ownership percentage of 61.9% until the equity security investment was also reduced to zero during the remaining period of 2019. BridgeBio's share of net losses for the year ended December 31, 2019 was not material. The carrying amount of BridgeBio's investment in PellePharm in the consolidated balance sheets through March 31, 2021 represented its maximum loss exposure related to its VIE investment in PellePharm. There were no impairments related to our PellePharm investment through March 31, 2021.

LEO terminated the LEO Agreement effective as of April 15, 2021. The date the LEO Agreement was terminated was determined to be a VIE reconsideration event. Based on our assessment, we continue to conclude that PellePharm remains a VIE after the reconsideration event as it does not have sufficient equity at risk to finance its activities without additional subordinated financial support. Based on the changes to PellePharm's board of directors composition as a result of the termination of the LEO Agreement, BridgeBio became the primary beneficiary as it has the power over the key decisions that most significantly impact PellePharm's economic performance and it has the obligation to absorb losses or the right to receive benefits from PellePharm that could potentially be significant to PellePharm through its common and preferred stock interest in PellePharm. Accordingly, BridgeBio consolidated PellePharm effective on April 15, 2021.

8. Intangible Assets

The following table summarizes our recognized intangible assets for the year ended December 31, 2022 and 2021 as a result of the arrangements described in the following sections:

	December 31, 2022		December 31, 2021	
	Weighted-average Estimated Useful Lives	Amount (in thousands)	Weighted-average Estimated Useful Lives	Amount (in thousands)
Gross amount	12.0 years	$ 32,500	12.8 years	$ 47,500
Less: accumulated amortization		(3,788)		(2,566)
Total		$ 28,712		$ 44,934

We had no intangible assets as of December 31, 2020. Amortization expense recorded as part of cost of license revenue and products sold for the years ended December 31, 2022 and 2021 was $2.4 million and $2.6 million, respectively. Future amortization expense is $2.4 million for each of the years from 2023 to 2026 and $19.1 million thereafter.

Novartis License Agreement

In January 2018, QED entered into a License Agreement with Novartis International Pharmaceutical, Inc. or Novartis, pursuant to which QED acquired certain intellectual property rights, including patents and know-how, related to infigratinib for the treatment of patients with FGFR-driven diseases. QED accounted for the transaction as an asset acquisition as substantially all of the estimated fair value of the gross assets acquired was concentrated in a single identified asset, in-process research and development, or IPR&D, thus satisfying the requirements of the screen test in ASU 2017-01, *Business Combinations (Topic 805), Clarifying the Definition of a Business*. The assets acquired and liabilities assumed in the transaction were measured based on their fair values. The fair value of the IPR&D acquired was charged to research and development expense as it had no alternative future use at the time of the acquisition.

If certain substantial milestones are met, QED could be required to pay up to $60.0 million in regulatory milestone payments, $35.0 million in sales-based milestone payments, and pay royalties of up to low double-digit percentages on net sales. Following the FDA approval of TRUSELTIQ™ in May 2021, we paid a one-time regulatory milestone payment to Novartis of $20.0 million. We capitalized such payment as a finite-lived intangible asset and amortize the amount over its estimated useful life on a straight-line basis.

Asset Purchase Agreement with Alexion

In June 2018, our subsidiary Origin Biosciences, Inc., or Origin, entered into an Asset Purchase Agreement with Alexion Pharma Holding Unlimited Company, or Alexion, to acquire intellectual property rights, including patent rights, know-how, and contracts, related to the ALXN1101 molecule. Origin accounted for the transaction as an asset acquisition as substantially all of the estimated fair value of the gross assets acquired was concentrated in a single identified asset, or IPR&D, thus satisfying the requirements of the screen test in ASU 2017-01. The assets acquired and liabilities assumed in the transaction were measured based on their fair values. The fair value of the IPR&D acquired was charged to research and development expense as it had no alternative future use at the time of the acquisition.

Pursuant to the Asset Purchase Agreement, Origin could be required to pay up to $18.8 million if a certain condition is met. Such a condition was met in 2021, resulting in a one-time final payment of $15.0 million, which we capitalized as a finite-lived intangible asset and amortize it over its estimated useful life on a straight-line basis. In addition, under the Asset Purchase Agreement, Origin could be required to pay up to $17.0 million in sales-based milestone payments and royalties of up to low double-digit percentages on net sales.

In connection with the Asset Purchase Agreement entered between Origin and Sentynl Therapeutics, Inc., or Sentynl, in March 2022, or the Origin-Sentynl APA, (see Note 12), Sentynl assumed the obligation to pay sales-based milestone payments and royalties to Alexion that occur subsequent to the closing of the Origin-Sentynl APA when they become due. Origin will continue to be responsible for a regulatory-based milestone payment upon first pricing approval in a European Medicines Agency, or EMA, country of up to $1.0 million when it becomes due. As a result of the Origin-Sentynl APA, we also derecognized the associated intangible asset with a net book value of $13.5 million as this was part of the assets that were transferred to Sentynl.

Diagnostics Agreement with Foundation Medicine

In November 2018, QED and Foundation Medicine, Inc., or FMI, entered into a companion diagnostics agreement relating to QED's drug discovery and development initiatives. Pursuant to the agreement, QED could be required to pay $12.5 million in regulatory approval milestones over a period of four years subsequent to the FDA approval of a companion diagnostic for TRUSELTIQ in patients with cholangiocarcinoma. The FDA approved the companion diagnostic for TRUSELTIQ in May 2021, which resulted in the capitalization of $12.5 million as a finite-lived intangible asset to be amortized over its estimated useful life on a straight-line basis. As of December 31, 2022, the amount due to FMI is presented in our consolidated balance sheet in "Other accrued liabilities" and "Other long-term liabilities" for $2.5 million and $8.5 million, respectively. As of December 31, 2021, the amount due to FMI is presented in our consolidated balance sheet in "Other accrued liabilities" for $1.5 million and "Other long-term liabilities" for $11.0 million.

9. Commitments and Contingencies

Milestone Compensation Arrangements

We have performance-based milestone compensation arrangements with certain employees and consultants, whose vesting is contingent upon meeting various milestones, with fixed monetary amounts known at inception that can be settled in the form of cash or equity at our sole discretion. We also have performance-based milestone compensation arrangements with certain employees and consultants as part of the 2020 Stock and Equity Award Exchange Program, or the Exchange Program, see Note 16. The compensation arrangements under the Exchange Program are to be settled in the form of equity only. Performance-based milestone awards that are settled in the form of equity are satisfied in the form of fully-vested restricted stock awards, or RSAs. We accrue for such contingent compensation when the related milestone is probable of achievement and is recorded in "Accrued compensation and benefits" for the current portion and in "Other long-term liabilities" for the noncurrent portion in the consolidated balance sheets. There is no accrued compensation expense for performance-based milestone awards that are assessed to be not probable of achievement. The table below shows our commitment for the potential milestone amounts and the accruals for milestones deemed probable of achievement as of December 31, 2022.

Settlement Type	Potential Fixed Monetary Amount	Accrued Amount (1)
	(in thousands)	
Cash	$ 10,142	$ 831
Stock (2)	60,558	9,716
Cash or stock at our sole discretion	103,072	2,080
Total	$ 173,772	$ 12,627

(1) Amount recorded for performance-based milestone awards that are probable of achievement.
(2) Includes the performance-based milestone awards that were granted as part of the Exchange Program further discussed in Note 16.

Other Research and Development and Commercial Agreements

We may also enter into contracts in the normal course of business with contract research organizations for clinical trials, with contract manufacturing organizations for clinical supplies, and with other vendors for preclinical studies, supplies, and other services and products for commercial and operating purposes. These contracts generally provide for termination on notice with potential termination charges. As of December 31, 2022, we have liabilities for certain fees that we have incurred related to reprioritization of our research and development projects of approximately $3.3 million (see Note 17). As of December 31, 2021, there were no material amounts accrued related to termination charges.

Indemnification

In the ordinary course of business, we may provide indemnifications of varying scope and terms to vendors, lessors, business partners, board members, officers, and other parties with respect to certain matters, including, but not limited to, losses arising out of breach of such agreements, services to be provided by us, our negligence or willful misconduct, violations of law, or intellectual property infringement claims made by third parties. In addition, we have entered into indemnification agreements with directors and certain officers and employees that will require us, among other things, to indemnify them against certain liabilities that may arise by reason of their status or service as directors, officers, or employees. No material demands have been made upon us to provide indemnification under such agreements, and thus, there are no claims that we are aware of that could have a material effect on our consolidated financial statements.

We also maintain director and officer insurance, which may cover certain liabilities arising from our obligation to indemnify our directors. To date, we have not incurred any material costs and have not accrued any liabilities in the consolidated financial statements as a result of these provisions.

Contingencies

From time to time, we may become involved in legal proceedings arising in the ordinary course of business. We are not currently a party to any material legal proceedings.

10. Debt

Notes

<u>*2029 Notes*</u>

On January 28, 2021, we issued an aggregate of $717.5 million principal amount of our 2029 Notes pursuant to an Indenture dated January 28, 2021, or the 2029 Notes Indenture, between us and U.S. Bank National Association, as trustee, or the 2029 Notes Trustee, in a private offering to qualified institutional buyers, or the 2021 Note Offering, pursuant to Rule 144A under the Securities Act of 1933, as amended, or the Securities Act. The 2029 Notes issued in the 2021 Note Offering include $67.5 million aggregate principal amount of 2029 Notes sold to the initial purchasers, or the 2029 Notes Initial Purchasers, pursuant to the exercise in part of the 2029 Notes Initial Purchasers' option to purchase $97.5 million principal amount of additional 2029 Notes. On January 28, 2021, the 2029 Notes Initial Purchasers exercised the remaining portion of their option to purchase $30.0 million principal amount of additional 2029 Notes. The sale of those additional 2029 Notes closed on February 2, 2021, which resulted in the total aggregate principal amount of $747.5 million.

The 2029 Notes are senior, unsecured obligations of BridgeBio and will accrue interest payable semiannually in arrears on February 1 and August 1 of each year, beginning on August 1, 2021, at a rate of 2.25% per year. The 2029 Notes will mature on February 1, 2029, unless earlier converted, redeemed or repurchased. The 2029 Notes are convertible into cash, shares of BridgeBio's common stock, or a combination of cash and shares of BridgeBio's common stock, at our election.

We received net proceeds from the 2021 Note Offering of approximately $731.4 million, after deducting the 2029 Notes Initial Purchasers' discount (there were no direct offering expenses borne by us for the 2029 Notes). We used approximately $61.3 million of the net proceeds from the 2021 Note Offering to pay for the cost of the 2021 Capped Call Transactions described below and approximately $50.0 million to pay for the repurchase of shares of BridgeBio common stock described below.

A holder of 2029 Notes may convert all or any portion of its 2029 Notes at its option at any time prior to the close of business on the business day immediately preceding November 1, 2028, in multiples of $1,000 only under the following circumstances:

- During any calendar quarter commencing after the calendar quarter ending on June 30, 2021 (and only during such calendar quarter), if the last reported sale price of BridgeBio's common stock for at least 20 trading days (whether or not consecutive) during a period of 30 consecutive trading days ending on, and including, the last trading day of the immediately preceding calendar quarter is greater than or equal to 130% of the conversion price on each applicable trading day;
- During the five-business day period after any five consecutive trading day period, or the measurement period, in which the "trading price" (as defined in the 2029 Notes Indenture) per $1,000 principal amount of 2029 Notes for each trading day of the measurement period was less than 98% of the product of the last reported sale price of BridgeBio's common stock and the conversion rate on each such trading day;
- If we call such notes for redemption, at any time prior to the close of business on the second business day immediately preceding the redemption date; or
- Upon the occurrence of specified corporate events, as defined in the 2029 Notes Indenture.

On or after November 1, 2028 until the close of business on the second scheduled trading day immediately preceding the maturity date, a holder may convert all or any portion of its 2029 Notes at any time, regardless of the foregoing.

The conversion rate will initially be 10.3050 shares of BridgeBio's common stock per $1,000 principal amount of 2029 Notes (equivalent to an initial conversion price of approximately $97.04 per share of BridgeBio's common stock, for a total of approximately 7,702,988 shares).

The conversion rate is subject to adjustment in some events but will not be adjusted for any accrued and unpaid interest. In addition, following certain corporate events that occur prior to the maturity date or if we deliver a notice of redemption, we will, in certain circumstances, increase the conversion rate for a holder who elects to convert its 2029 Notes in connection with such a corporate event. The maximum number of shares issuable should there be an increase in the conversion rate is 11,361,851 shares of BridgeBio's common stock.

We may not redeem the 2029 Notes prior to February 6, 2026. We may redeem for cash all or any portion of the 2029 Notes, at our option, on a redemption date occurring on or after February 6, 2026 and on or before the 41st scheduled trading day immediately before the maturity date, under certain circumstances. No sinking fund is provided for the Notes. If we undergo a fundamental change (as defined in the 2029 Notes Indenture), holders may require us to repurchase for cash all or any portion of their 2029 Notes at a fundamental change repurchase price equal to 100% of the principal amount of the 2029 Notes to be repurchased, plus any accrued and unpaid interest to, but excluding, the fundamental change repurchase date. The 2029 Notes Indenture contains customary terms and covenants, including that upon certain events of default occurring and continuing, either the 2029 Notes Trustee or the holders of not less than 25% in aggregate principal amount of the 2029 Notes then outstanding may declare the entire principal amount of all the Notes plus accrued special interest, if any, to be immediately due and payable. The 2029 Notes are our general unsecured obligations and rank senior in right of payment to all of our indebtedness that is expressly subordinated in right of payment to the 2029 Notes; equal in right of payment with all of our liabilities that are not so subordinated, including our 2027 Notes; effectively junior to any of our secured indebtedness to the extent of the value of the assets securing such indebtedness; and structurally junior to all indebtedness and other liabilities (including trade payables) of our subsidiaries.

In connection with the issuance of the 2029 Notes, we incurred approximately $16.1 million of debt issuance costs, which consisted of initial purchasers' discounts. This was recorded as a reduction in the carrying value of the debt on the consolidated balance sheet and is amortized to interest expense using the effective interest method over the expected life of the 2029 Notes or approximately their eight-year term.

2027 Notes

On March 9, 2020, we issued an aggregate principal amount of $550.0 million of our 2.50% Convertible Senior Notes due 2027, or the 2027 Notes, pursuant to an Indenture dated March 9, 2020, or the 2027 Notes Indenture, between us and U.S. Bank National Association, as trustee (the “2027 Notes Trustee”), in a private offering to qualified institutional buyers, or the 2020 Note Offering, pursuant to Rule 144A under the Securities Act. The 2027 Notes issued in the 2020 Note Offering include $75.0 million in aggregate principal amount of 2027 Notes sold to the initial purchasers, or the 2027 Notes Initial Purchasers, resulting from the exercise in full of their option to purchase additional 2027 Notes.

The 2027 Notes will accrue interest payable semiannually in arrears on March 15 and September 15 of each year, beginning on September 15, 2020, at a rate of 2.50% per year. The 2027 Notes will mature on March 15, 2027, unless earlier converted or repurchased. The 2027 Notes are convertible into cash, shares of BridgeBio’s common stock or a combination of cash and shares of BridgeBio’s common stock, at our election.

We received net proceeds from the 2020 Note Offering of approximately $537.0 million, after deducting the 2027 Notes Initial Purchasers’ discount and offering expenses. We used approximately $49.3 million of the net proceeds from the 2020 Note Offering to pay for the cost of the 2020 Capped Call Transactions described below, and approximately $75.0 million to pay for the repurchase of shares of BridgeBio common stock described below.

A holder of 2027 Notes may convert all or any portion of its 2027 Notes at its option at any time prior to the close of business on the business day immediately preceding December 15, 2026, in multiples of $1,000 only under the following circumstances:

- During any calendar quarter commencing after the calendar quarter ending on June 30, 2020 (and only during such calendar quarter), if the last reported sale price of BridgeBio’s common stock for at least 20 trading days (whether or not consecutive) during a period of 30 consecutive trading days ending on, and including, the last trading day of the immediately preceding calendar quarter is greater than or equal to 130% of the conversion price on each applicable trading day (the "Conversion Price Condition");
- During the five-business day period after any five consecutive trading day period, or the measurement period, in which the “trading price” (as defined in the Indenture) per $1,000 principal amount of 2027 Notes for each trading day of the measurement period was less than 98% of the product of the last reported sale price of BridgeBio’s common stock and the conversion rate on each such trading day; or,
- Upon the occurrence of specified corporate events, as defined in the 2027 Notes Indenture.

On or after December 15, 2026 until the close of business on the second scheduled trading day immediately preceding the maturity date, a holder may convert all or any portion of its 2027 Notes at any time, regardless of the foregoing.

Only during each of the calendar quarters ended March 31, 2021 and June 30, 2021, the 2027 Notes were eligible for conversion at the option of the holders as the Conversion Price Condition was met during the period. The Conversion Price Condition was not met for any other period during fiscal years 2022 and 2021.

The conversion rate will initially be 23.4151 shares of BridgeBio’s common stock per $1,000 principal amount of 2027 Notes (equivalent to an initial conversion price of approximately $42.71 per share of BridgeBio’s common stock, for a total of approximately 12,878,305 shares).

The conversion rate is subject to adjustment in some events but will not be adjusted for any accrued and unpaid interest. In addition, following certain corporate events that occur prior to the maturity date, we will, in certain circumstances, increase the conversion rate for a holder who elects to convert its 2027 Notes in connection with such a corporate event. The maximum number of shares issuable should there be an increase in the conversion rate is 17,707,635 shares of BridgeBio’s common stock.

We may not redeem the 2027 Notes prior to the maturity date, and no sinking fund is provided for the 2027 Notes. If we undergo a fundamental change (as defined in the 2027 Notes Indenture), holders may require us to repurchase for cash all or any portion of their 2027 Notes at a fundamental change repurchase price equal to 100% of the principal amount of the 2027 Notes to be repurchased, plus any accrued and unpaid interest to, but excluding, the fundamental change repurchase date. The 2027 Notes Indenture contains customary terms and covenants, including that upon certain events of default occurring and continuing, either the 2027 Notes Trustee or the holders of not less than 25% in aggregate principal amount of the 2027 Notes then outstanding may declare the entire principal amount of all the 2027 Notes plus accrued special interest, if any, to be immediately due and payable. The 2027 Notes are our general unsecured obligations and rank senior in right of payment to all of our indebtedness that is expressly subordinated in right of payment to the 2027 Notes; equal in right of payment with all of BridgeBio's liabilities that are not so subordinated, including our 2029 Notes; effectively junior to any of BridgeBio's secured indebtedness to the extent of the value of the assets securing such indebtedness; and structurally junior to all indebtedness and other liabilities (including trade payables) of our subsidiaries.

In accounting for the issuance of the 2027 Notes in 2020 under ASC 470-20, *Debt: Debt with Conversion and Other Options*, we separately accounted for the liability and equity components of the 2027 Notes by allocating the proceeds between the liability component and the embedded conversion options, or equity component, due to our ability to settle the 2027 Notes in cash, BridgeBio common stock, or a combination of cash and BridgeBio common stock at our option. Effective January 1, 2021, we early adopted ASU 2020-06, *Debt – Debt with Conversion and Other Options (Subtopic 470-20) and Derivatives and Hedging – Contracts in Entity's Own Equity (Subtopic 815-40): Accounting for Convertible Instruments and Contracts in an Entity's Own Equity,* and, as a result, we no longer separately account for the liability and equity components of the 2027 Notes, and, instead, account for our 2027 Notes wholly as debt.

In connection with the issuance of the 2027 Notes, we incurred approximately $13.0 million of debt issuance costs, which primarily consisted of initial purchasers' discounts and legal and other professional fees. We allocated these costs to the liability and equity components based on the allocation of the proceeds. The portion of these costs allocated to the equity component totaling approximately $4.1 million was recorded as a reduction to additional paid-in capital in 2020. The portion of these costs allocated to the liability component totaling approximately $8.9 million was recorded as a reduction in the carrying value of the debt on the consolidated balance sheet and was amortized to interest expense using the effective interest method over the expected life of the 2027 Notes or approximately their seven-year term.

Additional Information Related to the Notes

The outstanding Notes' balances consisted of the following:

	December 31, 2022		December 31, 2021	
	2029 Notes	2027 Notes	2029 Notes	2027 Notes
	(in thousands)		(in thousands)	
Principal	$ 747,500	$ 550,000	$ 747,500	$ 550,000
Unamortized debt discount and issuance costs	(12,512)	(8,366)	(14,381)	(10,066)
Net carrying amount	$ 734,988	$ 541,634	$ 733,119	$ 539,934

The following table sets forth the total interest expense recognized and effective interest rates related to the Notes:

	Year ended December 31, 2022			Year ended December 31, 2021			Year ended December 31, 2020
	2029 Notes	2027 Notes	Total	2029 Notes	2027 Notes	Total	2027 Notes
	(in thousands)						
Contractual interest expense	$ 16,819	$ 13,750	$ 30,569	$ 15,557	$ 13,750	$ 29,307	$ 11,153
Amortization of debt discount and issuance costs	1,869	1,699	3,568	1,682	1,654	3,336	15,649
Total interest and amortization expense	$ 18,688	$ 15,449	$ 34,137	$ 17,239	$ 15,404	$ 32,643	$ 26,802
Effective interest rate	2.6 %	2.8 %		2.6 %	2.8 %		8.8 %

As of December 31, 2022, interest payable on the 2029 and 2027 Notes amounted to $7.0 million and $4.0 million, respectively. As of December 31, 2021, interest payable on the 2029 and 2027 Notes amounted to $7.0 million and $4.0 million, respectively. Such amounts are included in “Other accrued liabilities” in our consolidated balance sheets.

Future minimum payments under the Notes as of December 31, 2022, are as follows:

	2029 Notes	2027 Notes	Total
		(in thousands)	
Year ending December 31:			
2023	$ 16,819	$ 13,750	$ 30,569
2024	16,819	13,750	30,569
2025	16,819	13,750	30,569
2026	16,819	13,750	30,569
2027	16,819	556,875	573,694
Thereafter	772,728	—	772,728
Total future payments	856,823	611,875	1,468,698
Less amounts representing interest	(109,323)	(61,875)	(171,198)
Total principal amount	$ 747,500	$ 550,000	$ 1,297,500

Capped Call and Share Repurchase Transactions with Respect to the Notes

On each of January 25, 2021 and March 4, 2020, concurrently with the pricing of the 2029 Notes and 2027 Notes, respectively, we entered into separate privately negotiated capped call transactions (the "2021 Capped Call Transactions" and the "2020 Capped Call Transactions", respectively), or, together, the Capped Call Transactions, with certain financial institutions, or the Capped Call Counterparties. We used approximately $61.3 million and $49.3 million of the net proceeds from the 2021 Note Offering and 2020 Note Offering, respectively, to pay for the cost of the respective Capped Call Transactions. The Capped Call Transactions are expected generally to reduce the potential dilution to BridgeBio's common stock upon any conversion of Notes and/or offset any cash payments we are required to make in excess of the principal amount of converted Notes, as the case may be, with such reduction and/or offset subject to a cap initially equal to $131.58 for the 2021 Capped Call Transactions and $62.12 for the 2020 Capped Call Transactions (both of which represented a premium of 100% over the last reported sale price of BridgeBio's common stock on the date of the Capped Call Transactions) and are subject to certain adjustments under the terms of the Capped Call Transactions. The 2021 Capped Calls and 2020 Capped Calls cover 7,702,988 shares and 12,878,305 shares, respectively, of our common stock (subject to anti-dilution and certain other adjustments), which are the same number of shares of common stock that initially underlie the Notes. The 2021 Capped Calls have an initial strike price of approximately $97.04 per share, which corresponds to the initial conversion price of the 2029 Notes. The 2020 Capped Calls have an initial strike price of approximately $42.71 per share, which corresponds to the initial conversion price of the 2027 Notes. The Capped Call Transactions are separate transactions, entered into by us with the Capped Call Counterparties, and are not part of the terms of the Notes.

These Capped Call instruments meet the conditions outlined in ASC 815-40, *Derivatives and Hedging,* to be classified in stockholders' equity and are not subsequently remeasured as long as the conditions for equity classification continue to be met. We recorded a reduction to additional paid-in capital of approximately $61.3 million and $49.3 million for the years ended December 31, 2021 and 2020, respectively, related to the premium payments for the Capped Call Transactions.

Additionally, we used approximately $50.0 million and $75.0 million of the net proceeds from the 2021 Note Offering and 2020 Note Offering to repurchase 759,993 shares and 2,414,681 shares, respectively, of our common stock concurrently with the closing of the Note Offerings from certain of the Notes' Initial Purchasers in privately negotiated transactions. The agreed purchase price per share of common stock in the repurchases were $65.79 and $31.06, which were the last reported sale prices per share of our common stock on The Nasdaq Global Select Market, or Nasdaq, on January 25, 2021 and March 4, 2020, respectively. The shares repurchased were recorded as treasury stock.

Term Loan

Loan and Security Agreement

In November 2021, we entered into a Loan and Security Agreement, or the Loan Agreement, by and among (i) U.S. Bank National Association, in its capacity as administrative agent, or, in such capacity, the Administrative Agent, and collateral agent, or, in such capacity, the Collateral Agent, (ii) certain lenders, or the Lenders, (iii) BridgeBio, as a borrower, and (iv) certain subsidiaries of BridgeBio, as guarantors, or the Guarantors. In May 2022, we entered into the First Amendment to the Loan Agreement, or the First Amendment, and in November 2022, we entered into the Second Amendment to the Loan Agreement, or the Second Amendment, as further described below.

Pursuant to the original terms and conditions of the Loan Agreement, the Lenders agreed to extend term loans to us in an aggregate principal amount of up to $750.0 million, comprised of (i) a tranche 1 advance of $450.0 million, or the Tranche 1 Advance, and (ii) a tranche 2 advance of $300.0 million, or the Tranche 2 Advance or collectively, the Term Loan Advances. The Tranche 1 Advance under the Loan Agreement was funded on November 17, 2021. The Tranche 2 Advance remained available for funding until December 31, 2022, which was available at our election after the occurrence of certain milestone events relating to data from our clinical trials. The terms related to the Tranche 2 Advance were modified in the First Amendment and Second Amendment as further discussed below. The First Amendment's term included the reduction of the aggregate amount of the Tranche 2 Advance from $300.0 million to $100.0 million. The Second Amendment eliminated the $100.0 million Tranche 2 Advance. As a result of the Second Amendment, the total aggregate principal amount of the loan is $450.0 million before any mandatory prepayment.

As security for our obligations under the Loan Agreement, each of BridgeBio and the Guarantors granted the Collateral Agent, for the benefit of the Lenders, a continuing security interest in substantially all of the assets of BridgeBio and the Guarantors (including all equity interests owned or hereafter acquired by BridgeBio and the Guarantors), subject to certain customary exceptions. Upon exceeding certain investment and disposition thresholds, additional subsidiaries of BridgeBio will be required to join as guarantors.

Any outstanding principal on the Term Loan Advances will accrue interest at a fixed rate equal to 9.0% per annum, 3.0% of which can be paid in kind, or PIK, until January 1, 2025. Interest payments are payable quarterly following the funding of a Term Loan Advance. We will be required to make principal payments on the outstanding balance of the Term Loan Advances commencing on January 2, 2025, or the Term Loan Amortization Date, in nine quarterly installments, plus interest. If we have achieved certain milestone events relating to data from the clinical trial of acoramidis, or the Acoramidis Milestone, on or prior to January 1, 2025, then the Term Loan Amortization Date will be automatically extended to January 2, 2026. Any amounts outstanding under the Term Loan Advances are due and payable on November 17, 2026, or the Maturity Date.

We may prepay the outstanding principal amount of the Term Loan Advances at any time (in whole, but not in part), plus accrued and unpaid interest and a prepayment premium ranging from 1.0% to 3.0% of the principal amount outstanding depending on the timing of payment (plus a customary make-whole amount if prepaid on or prior to November 17, 2022).

At the Lenders' election, we are also required to make mandatory prepayments upon the occurrence of certain prepayment events related to the repurchase or redemption of pledged collateral, entry into certain royalty transactions, disposition of other assets or subsidiaries, and entry into licensing and other monetization transactions (all such events "prepayment events"), which could be 50.0% or 75.0% of net cash proceeds from such transaction depending on achievement of the Acoramidis Milestone.

Subject to the mandatory prepayment requirements for certain prepayment events, the Loan Agreement contains customary affirmative and limited negative covenants which, among other things, limit our ability to (i) incur additional indebtedness, (ii) pay dividends or make certain distributions, (iii) dispose of our assets, grant liens, license or encumber our assets or (iv) fundamentally alter the nature of our business. BridgeBio and the Guarantors have broad ability to license our intellectual property, dispose of other assets and enter into monetization and royalty transactions, subject in each case to the requirement to make a mandatory prepayment described above. The Loan Agreement provides that BridgeBio and the Guarantors may, subject to certain limitations, (x) repurchase the BridgeBio's equity interest and the equity interest of any of its subsidiaries, (y) enter into any joint ventures or similar investments, and (z) make other investments and acquisitions. Subject to the mandatory prepayment requirement described above, portfolio companies owned by BridgeBio that are not parties to the Loan Agreement are, subject to certain exceptions, not subject to any covenants or limitations under the Loan Agreement.

The Loan Agreement also contains customary events of default, including among other things, our failure to make any principal or interest payments when due, the occurrence of certain bankruptcy or insolvency events or the breach of the covenants under the Loan Agreement. Upon the occurrence of an event of default, the Lenders may, among other things, accelerate our obligations under the Loan Agreement.

We received net proceeds from the Tranche 1 Advance of $431.3 million, after deducting debt discount and issuance costs of $18.7 million, of which approximately $1.1 million of debt issuance cost were incurred for professional services provided by KKR Capital Markets LLC. KKR Capital Markets LLC is an affiliate of KKR Genetic Disorder L.P., a related party being a principal stockholder of BridgeBio.

In May 2022, we entered into the First Amendment, which, among other things:

- permitted the sale of our priority review voucher, or PRV, see Note 12 and, generally, future dispositions of other PRVs;
- reduced the aggregate amount of the Tranche 2 Advance from $300.0 million to $100.0 million and modified certain conditions to the availability thereof, as mentioned above;
- amended the principal payments such that the entire outstanding principal balance of the Term Loan Advances is due and payable at the Maturity Date or upon early termination; and
- modified the terms and conditions governing when certain entities into which we have made investments will be required to become guarantors under the Amended Loan Agreement.

In June 2022, the receipt of an upfront payment under the Navire-BMS License Agreement, which is further described in Note 11, triggered certain mandatory prepayment provisions of the Amended Loan Agreement. As a result, we paid $20.5 million to the Lenders, of which $20.1 million and $0.4 million were applied to principal and exit fee, respectively.

Pursuant to the terms of the Loan Agreement and the Amended Loan Agreement, we exercised our option to convert accrued interest into principal via PIK amounting to $15.3 million for the year ended December 31, 2022.

In November 2022, we entered into the Second Amendment, which, among other things:

- acknowledged that the Company's prior prepayment made with certain cash proceeds received in connection the receipt of an upfront payment under the Navire-BMS License Agreement, which is further described in Note 11, satisfied the mandatory prepayment requirement under the Amended Loan Agreement, on the terms and conditions specified in the Amended Loan Agreement;
- permitted certain budgeted expenses to be excluded from the definition of cash proceeds subject to the Company's mandatory prepayment obligations, on the terms and conditions specified in the Amended Loan Agreement, refer to Note 2 under Restricted Cash section for further discussion.
- removed certain threshold amounts applicable to certain prepayment events; and
- terminated the Lenders' $100.0 million Tranche 2 Advance.

For the year ended December 31, 2022, we recognized interest expense related to the Loan Agreement of $46.1 million, of which $5.0 million, relates to amortization of debt discount and issuance costs. For the year ended December 31, 2021, we recognized interest expense related to the Loan Agreement of $5.5 million, of which $0.6 million, relates to amortization of debt discount and issuance costs. As of December 31, 2022 and 2021, interest payable included in "Other accrued liabilities" in our consolidated balance sheets amounted to $6.4 million and $5.0 million, respectively.

The following table summarizes our term loans:

	December 31, 2022	December 31, 2021
	(in thousands)	
Principal value of term loans	$ 429,916	$ 450,000
PIK added to principal	15,324	—
Debt discount, issuance costs and exit fees accretion	(14,247)	(19,248)
Term loan, net	$ 430,993	$ 430,752

Future minimum payments under the Loan Agreement as of December 31, 2022, are as follows:

	Amount (in thousands)
Year Ending December 31:	
2023	$ 37,051
2024	40,628
2025	40,628
2026	499,698
Total future payments	618,005
Less amounts representing interest	(164,167)
Less exit fee	(8,598)
Total principal amount of term loan payments	$ 445,240

Hercules Loan and Security Agreement

We had a Loan and Security Agreement, as amended from time to time, with Hercules Capital, Inc., or Hercules, or the Hercules Term Loan, under which we borrowed principal amounts of $35.0 million, or Tranche I, $20.0 million, or Tranche II, $20.0 million, or Tranche III, and $25.0 million, or Tranche IV.

In January 2021, we executed the Fifth Amendment to the Loan and Security Agreement primarily to allow us to issue our 2029 Notes and to enter into the related 2021 Capped Call and share repurchase transactions.

In April 2021, we executed the Sixth Amendment to the Loan and Security Agreement, or the Amended Hercules Term Loan.

The Amended Hercules Term Loan was prepaid in full in November 2021 using a portion of the net proceeds from the Tranche 1 Advance under the Loan Agreement mentioned above, which resulted in a loss on early extinguishment of debt of $2.6 million that is included in “Other income (expense)” in our consolidated statements of operations. For the years ended December 31, 2021, and 2020, we recognized interest expense related to the Amended Hercules Term Loan of $8.1 million and $7.9 million, respectively, of which $1.7 million and $1.3 million, respectively, relates to amortization of debt discount and issuance costs.

Silicon Valley Bank and Hercules Loan and Security Agreement

Eidos entered into a Loan and Security Agreement with Silicon Valley Bank, or SVB, and Hercules Capital, Inc. or the SVB and Hercules Loan Agreement, under which Eidos borrowed a principal amount of $17.5 million, or the Tranche A Loan, in November 2019. The Tranche A Loan was subject to an interest rate equal to the greater of either (i) 8.50% or (ii) 3.25% plus the prime rate as reported in The Wall Street Journal (8.50% during the relevant period in 2021) and had an original maturity date of October 2, 2023.

The Tranche A Loan was prepaid in full in April 2021 for $18.1 million, which includes a final payment charge and a prepayment fee, using a portion of the proceeds from Tranche IV under the Amended Hercules Term Loan discussed above. Loss on early extinguishment of the Tranche A Loan recognized by Eidos was not material. Interest expense on the Tranche A Loan was not material in 2021 through the prepayment date.

11. License and Collaboration Agreements

License Development and Commercialization Agreement with BMS

On May 12, 2022, BridgeBio and our subsidiary, Navire Pharma, Inc., or Navire, entered into an exclusive license development and commercialization agreement with BMS, or the Navire-BMS License Agreement, pursuant to which Navire granted BMS exclusive rights to develop and commercialize Navire’s product candidate, BBP-398, in all indications worldwide, except for the People’s Republic of China, Macau, Hong Kong, Taiwan, Thailand, Singapore, and South Korea, or the Asia Region. The development and commercialization of BBP-398 within the Asia Region is governed under the Navire-LianBio License Agreement (as discussed below). The Navire-BMS License Agreement expands an earlier agreement between Navire and BMS that was executed in July 2021 to study BBP-398 in a combination therapy trial to treat advanced solid tumors with KRAS mutations, or the 2021 Navire-BMS Agreement. The Navire-BMS License Agreement does not alter the terms of the 2021 Navire-BMS Agreement.

Under the terms of the Navire-BMS License Agreement, Navire was entitled to receive a non-refundable, upfront payment of $90.0 million, which Navire collected in full in June 2022. Additionally, Navire is eligible to receive additional payments totaling up to approximately $815.0 million in the aggregate, subject to the achievement of development, regulatory and commercial milestones, as well as tiered royalties in the low-to-mid teens as a percentage of adjusted net sales by BMS of the licensed products sold worldwide, outside of the Asia Region. Navire will retain the option to acquire higher royalties in the United States in connection with funding a portion of development costs upon the initiation of registrational studies. Based on the terms of the Navire-BMS License Agreement, Navire will continue to lead its ongoing Phase 1 monotherapy and combination therapy trials collectively, the Phase 1 Trials, and BMS will lead and fund all other development and commercialization activities. Navire is fully funding the Phase 1 trials with the exception of the combination therapy governed under the 2021 Navire-BMS Agreement. In accordance with the 2021 Navire-BMS License Agreement, both parties are sharing all research and development costs equally for this trial. We have recorded all research and development costs for the Phase 1 Trials, as well as the reimbursement for the costs associated with the trial governed by the 2021 Navire-BMS Agreement within research and development in our consolidated statement of operations.

We determined that the Navire-BMS License Agreement falls within the scope of ASC 606 as BMS is a customer in this arrangement, and we identified the following performance obligations in the agreement:

- an exclusive license to develop and commercialize BBP-398 and the related know-how; and
- research and development services to complete the Phase 1 Trials for BBP-398 (expected to be completed in 2025).

We determined that the performance obligations outlined above are capable of being distinct and distinct within the context of the contract given such rights and activities are independent of each other. The license can be used by BMS without the research and development services. Similarly, those services provide a distinct benefit to BMS within the context of the contract, separate from the license, as the services could be provided by BMS or another third party without our assistance. Options for additional goods or services were not considered material rights as they were not offered at a discount, and as such not identified as performance obligations, at the inception of the Navire-BMS License Agreement.

We determined the initial transaction price at inception of the Navire-BMS License Agreement to be $90.0 million, which is comprised of the fixed and non-refundable upfront payment. No additional development, regulatory, or sales milestone payments are included in the transaction price, as all such payments are variable consideration that are fully constrained as of the inception of the agreement and as of December 31, 2022. We include variable consideration in our transaction price to the extent that it is probable that it will not result in a significant revenue reversal when the uncertainty associated with the variable consideration is subsequently resolved. As part of management's evaluation of the variable consideration, we considered numerous factors, including the fact that achievement of the milestones is outside of our control, contingent upon the success of our existing and future clinical trials, BMS' efforts, and receipt of regulatory approval that is subject to scientific risks of success. Royalty arrangements and commercial-based milestones will be recognized when the sales occur or the milestones are achieved pursuant to the sales-based royalty exception under ASC 606 because the license is the predominant item to which the royalties or commercial-based milestones relate. We will re-evaluate the transaction price at each reporting period and as uncertain events are resolved or other changes in circumstances occur.

We allocated the transaction price of $90.0 million based on the stand-alone selling prices, or SSP, of each of the performance obligations as follows:

- $70.2 million for the upfront transfer of the license; and
- $19.8 million for ongoing research and development services.

The SSP for the license was determined using an approach that considered discounted, probability-weighted cash flows related to the license transferred. The SSP for the ongoing research and development services were based on estimates of the associated effort and cost of these services, adjusted for a reasonable gross profit margin that would be expected to be realized under similar contracts.

We recognized revenue for each of the two performance obligations as follows:

- We recognized revenue related to the license at a point in time upon transfer of the rights and control of the license to BMS. The transfer of the rights and control of the license occurred in June 2022, thus we recognized the full amount allocated to the license and related know-how during the year ended December 31, 2022.
- The research and development services performance obligation consists of our completion of the Phase 1 Trials. We are recognizing revenue related to the research and development services over time using an input method to measure progress by utilizing costs incurred to-date relative to total expected costs. We expect to complete the Phase 1 Trials in 2025. Revenue recognized related to this performance obligation for the year ended December 31, 2022 was $4.5 million.

For the year ended December 31, 2022, we recognized $74.7 million of revenue from the Navire-BMS License Agreement. Our consolidated balance sheet as of December 31, 2022 includes a deferred revenue balance of $15.3 million ($8.2 million presented as "Deferred revenue, current portion" and $7.1 million included in "Other long-term liabilities") related to our research and development services obligation.

License and Collaboration Agreement with Helsinn

On March 29, 2021, QED entered into a license and collaboration agreement with Helsinn Healthcare S.A. or HHC, and Helsinn Therapeutics (U.S.), Inc., or HTU, and collectively with HHC, Helsinn, or the QED-Helsinn License and Collaboration Agreement, pursuant to which QED granted to HHC exclusive licenses to develop, manufacture and commercialize QED’s product candidate, infigratinib, in oncology and all other indications except achondroplasia or any other skeletal dysplasias, worldwide, except for the People’s Republic of China, Hong Kong and Macau, or Greater China, and under which QED received a co-exclusive license to co-commercialize infigratinib in the United States in the licensed indications. Under this agreement, Helsinn is likewise entitled to a right of first negotiation with respect to specific territories subject to the occurrence of a contingent event. As part of this agreement, QED was also required to transfer inventory within the transitional period, as described in the QED-Helsinn License and Collaboration Agreement. The QED-Helsinn License and Collaboration Agreement became effective on April 16, 2021. Under the terms of the QED-Helsinn License and Collaboration Agreement, QED was eligible to receive payments totaling up to approximately $2.45 billion in the aggregate, including over $100.0 million in upfront, regulatory and launch milestone payments, and the remainder subject to the achievement of specified commercial milestones, as well as tiered royalties in the high teens as a percentage of adjusted net sales by Helsinn of the licensed products sold worldwide, outside of the United States and Greater China. Upon approval by the FDA, QED and HTU will co-commercialize infigratinib in the licensed indications in the United States and will share profits and losses on a 50:50 basis. In May 2021, we received such FDA approval for an oncology indication in the United States and effective as of that date, sharing of profits and losses commenced. QED and Helsinn will share global, excluding Greater China, research and development costs for infigratinib in the licensed indications at a rate of 40% for QED and 60% for Helsinn.

On February 28, 2022, QED and Helsinn amended the QED-Helsinn License and Collaboration Agreement, or the Amended QED-Helsinn License and Collaboration Agreement, effective as of March 1, 2022. Under the terms of the Amended QED-Helsinn License and Collaboration Agreement, Helsinn has an exclusive license to commercialize infigratinib in the U.S. and is responsible for developing, manufacturing and commercializing infigratinib in oncology indications except for achondroplasia or any other skeletal dysplasias worldwide, outside of Greater China. QED retains all rights to develop, manufacture and commercialize infigratinib in skeletal dysplasia, including achondroplasia.

Pursuant to the Amended QED-Helsinn License and Collaboration Agreement, QED no longer shared in the commercialization of infigratinib in the licensed indications in the United States or was responsible for any global development costs for infigratinib in the licensed indications.

Additionally, under the Amended QED-Helsinn License and Collaboration Agreement, QED was eligible to receive regulatory and sales-based milestone payments of up to $66.0 million, as well as tiered royalties in the low to mid-teens as a percentage of adjusted net sales by Helsinn of the licensed products sold worldwide, outside of Greater China.

The Amended QED-Helsinn License and Collaboration Agreement also provides for a transitional period, which extended from the effective date through August 31, 2022, for which QED was contracted to assist in research and development and commercialization activities. The costs related to QED's contracted activities incurred during the transitional period are fully reimbursable by Helsinn and will be paid to QED subsequent to the transitional period. Helsinn also agreed to reimburse QED’s obligation to FMI described in Note 8 as part of the Amended QED-Helsinn License and Collaboration Agreement. In recording the receivable, we recognized a corresponding gain that is recorded as part of “Other income (expense), net” in our consolidated statement of operations for the year ended December 31, 2022.

On August 23, 2022, we received written notice from Helsinn of its intent to terminate the Amended QED-Helsinn License and Collaboration Agreement for convenience, pursuant to its terms, citing commercial considerations. Effective December 21, 2022, QED and Helsinn, or the Helsinn Parties entered into a Mutual Termination Agreement, or MTA which terminates the Amended QED-Helsinn License and Collaboration Agreement and all rights and obligations thereunder. Under the terms of the MTA, the Helsinn Parties are responsible for performing certain close-out services to enable QED to pursue the development, manufacturing, and commercialization of infigratinib as a potential treatment of non-oncology indications, such as in achondroplasia worldwide, excluding China, Hong Kong, and Macau. Additionally, QED will no longer be entitled to any future regulatory or sales-based milestone payments and will continue to receive royalties on net sales of TRUSELTIQ until Helsinn no longer sells the licensed product by March 31, 2023. The Helsinn Parties delivered notice to the FDA notifying them that the distribution of TRUSELTIQ is permanently discontinued and that all clinical investigations under the associated IND are discontinued.

In accordance with the MTA, all outstanding obligations under the Amended QED-Helsinn License and Collaboration agreement related to the contracted services during the transitional period became due. This includes the reimbursable contracted research and development and commercial activities of $18.8 million and the reimbursement of QED’s obligation to FMI of $12.5 million described in Note 8. In accordance with the payment terms of the MTA, we received $15.0 million from Helsinn in December 2022. The remaining outstanding balance as of December 31, 2022 is $16.3 million and is presented in “Receivables from licensing and collaboration agreements” within our consolidated balance sheets. Of the receivable outstanding, $5.3 million was received in January 2023 and the remaining $11.0 million relates to the reimbursement of QED’s obligation to FMI which is due in eleven equal monthly installments commencing in February 2023.

All costs incurred subsequent to the transitional period are considered close-out costs and the responsibilities between the Helsinn Parties are outlined within the Close-Out Plan, as defined in the MTA. Activities within the Close-Out Plan are to be shared equally subsequent to the first $11.0 million of costs, which are the responsibility of QED, per the terms of the MTA. As of December 31, 2022, QED has incurred $11.0 million of costs relating to the Close-Out Plan. The activities within the Close-Out Plan are expected to be completed during 2023. All costs incurred, including Helsinn’s reimbursements, are recorded in "Restructuring, impairment and related charges" within our consolidated statement of operations. See Note 17.

Prior to the execution of the MTA, both the QED-Helsinn License and Collaboration Agreement and the Amended QED-Helsinn License and Collaboration Agreement were considered to be within the scope of ASC 808 as the parties are active participants and are exposed to the significant risks and rewards of the collaborative activity, and partially within the scope of ASC 606 for the units of account where Helsinn is identified as a customer. For the units of account in the collaboration arrangement that do not represent a vendor-customer relationship, including the performance of collaborative research and development and commercialization services, we determined that ASC 606 is not appropriate to apply by analogy and applied a reasonable and rational accounting policy election that faithfully depicts the transfer of services to the collaboration partner over the estimated performance period. Reimbursement payments from Helsinn associated with the collaborative research and development and commercialization services are recognized as the related expense is incurred and classified as an offset to the underlying expense and excluded from the transaction price.

We evaluated the terms of the QED-Helsinn License and Collaboration Agreement and identified Helsinn as a customer with the following two distinct performance obligations: (1) exclusive licenses to develop, manufacture, and commercialize the underlying product, and (2) transfer of inventory within the transitional supply period. The Amended QED-Helsinn License and Collaboration Agreement did not give rise to any additional performance obligations.

We determined the initial transaction price at inception of the QED-Helsinn License and Collaboration Agreement to be $46.0 million, comprised of a $20.0 million nonrefundable upfront license fee, $1.0 million for the sale of certain existing inventory, and a $25.0 million launch milestone for the first launch of the first indication of infigratinib in the United States. At the inception of the QED-Helsinn License and Collaboration Agreement we considered all future potential regulatory milestones to be variable consideration that are fully constrained . We determined that the achievements of such regulatory milestones are contingent upon success in future clinical trials and regulatory approvals, which are not within our control and are uncertain at the inception date. We constrain variable consideration to the extent that it is probable that it will not result in a significant revenue reversal when the uncertainty associated with the variable consideration is subsequently resolved. We recognize consideration related to sales-based milestone and royalties when the subsequent sales occur pursuant to the royalty exception under ASC 606 because the license is the predominant item to which the royalties or sales-based milestone relate. In the fourth quarter of 2021, we received validation from the EMA for our marketing authorization for infigratinib. Since the uncertainty of the variable consideration related to the regulatory milestone was resolved, we updated the transaction price to include this consideration, and accordingly, we increased our transaction price by $10.0 million to $56.0 million. The Amended QED-Helsinn License and Collaboration Agreement did not affect the transaction price as the modifications to the transaction price related solely to variable consideration, consisting of regulatory and sales-based milestone payments and royalties. The remaining future potential regulatory milestone payments did not result in a modification to the transactions price as the transaction price as they were determined to be fully constrained under ASC 606. QED began to receive royalties for net sales of the licensed products sold in the United States upon the effective date of the Amended QED-Helsinn License and Collaboration Agreement.

We allocated the $56.0 million transaction price based on relative SSPs of each of our performance obligations as $54.4 million for the licenses and $1.6 million for the transfer of inventory. For the delivery of the licenses, we based the SSP on a discounted cash flow approach and considered several factors including, but not limited to, forecasted revenue and costs, development timelines, discount rate and probabilities of clinical and regulatory success. For the transfer of inventory, we based the SSP on the actual costs incurred by us to purchase or manufacture the inventory as well as the average compensation of employees estimated to be incurred over the performance period.

As of December 31, 2021, we had provided all necessary information to Helsinn for it to benefit from the license under the license term and completed the transfer of inventory. During the year ended December 31, 2021, we recognized $56.0 million of license revenue, under these units of account accounted for under ASC 606.

For the unit of account that is within the scope of ASC 808 relating to collaborative research and development services, pursuant to the QED-Helsinn License and Collaboration Agreement, we have recognized Helsinn's share of research and development expenses of $2.9 million and $38.4 million as reduction of research and development expenses during the years ended December 31, 2022 and 2021, respectively, which represents 60% reimbursement of research and development expenses incurred. In accordance with the Amended QED-Helsinn License and Collaboration Agreement, we have recognized $18.6 million as reduction of research and development expenses for the year ended December 31, 2022, which represents 100% reimbursement of research and development costs incurred during the transitional period relating to infigratinib in the licensed indications.

Following the FDA approval of TRUSELTIQ in May 2021, we were the principal selling party of this product in the United States and recognized product sales in the consolidated statement of operations. Commencing in January 2022, we sold the remaining transitional supply of TRUSELTIQ to Helsinn, and Helsinn became the principal selling party. Accordingly, beginning in 2022, we no longer recognized product sales associated with TRUSELTIQ, although we continued to share losses on a 50:50 basis through February 28, 2022 in accordance with the QED-Helsinn License and Collaboration Agreement. Pursuant to the QED-Helsinn License and Collaboration Agreement, we accounted for Helsinn's share of the co-commercialization loss of $1.3 million and $8.9 million as reduction to selling, general and administrative expenses during the years ended December 31, 2022 and 2021, respectively. In accordance with the Amended QED-Helsinn License and Collaboration Agreement, we have recognized $0.2 million as a reduction to selling, general and administrative expenses during the year ended December 31, 2022, which represents 100% reimbursement of commercial activity costs incurred during the transitional period relating to infigratinib in the licensed indications in the United States.

License Agreements with LianBio

Navire

In August 2020, Navire entered into an exclusive license agreement with LianBio, or the Navire-LianBio License Agreement. Pursuant to the Navire-LianBio License Agreement, Navire granted to LianBio an exclusive, sublicensable license under the licensed patent rights and know-how to develop, manufacture and commercialize SHP2 inhibitor BBP-398, or BBP-398, for tumors driven by RAS and receptor tyrosine kinase mutations. Under the terms of the Navire-LianBio License Agreement, LianBio will receive commercial rights in China and selected Asian markets and participate in clinical development activities for BBP-398. In consideration for the rights granted to LianBio, we received a nonrefundable $8.0 million upfront payment, which we recognized as license revenue in 2020. We will also have the right to receive future development and sales milestone payments of up to $382.1 million, and tiered royalty payments from single-digit to low-teens on net sales of the product in licensed territories.

We accounted for the Navire-LianBio License Agreement under ASC 606 and identified the exclusive license as a distinct performance obligation since LianBio can benefit from the license on its own by developing and commercializing the underlying product using its own resources. In addition, we will enter into clinical and commercial supply agreements for the licensed territory. We determined that the optional right to future products under these supply agreements does not represent a material right. In July 2022, Navire and LianBio entered into a clinical supply agreement for the manufacture and supply of clinical quantities of the licensed product. During the year ended December 31, 2022, Navire has billed insignificant amounts to LianBio as part of the clinical supply agreement and recognized such amounts as license revenue.

In the second quarter of 2021, a development milestone became probable. Since the uncertainty of the variable consideration related to the development milestone was resolved, we updated the transaction price to include this consideration, and accordingly, we increased our transaction price by $8.5 million and recognized the entire amount as license revenue during the year ended December 31, 2021.

We consider the future potential development milestone as well as the sales-based royalties to be variable consideration. The future potential milestone payments were not included in the transaction price as they were all determined to be fully constrained under ASC 606. We determined that the achievements of such development milestones are contingent upon success in future clinical trials and regulatory approvals, which are not within our control and are uncertain at this stage. We expect that the royalty arrangements and sales-based milestones will be recognized when the sales occur or the milestones are achieved pursuant to the sales-based royalty exception under ASC 606 because the license is the predominant item to which the royalties or sales-based milestones relate. We will re-evaluate the transaction price at each reporting period and as uncertain events are resolved or other changes in circumstances occur.

QED

In October 2019, QED entered into an exclusive license agreement with LianBio (the "QED-LianBio License Agreement"). Pursuant to the QED-LianBio License Agreement, QED granted to LianBio an exclusive, sublicensable license under the licensed patent rights and know-how to develop, manufacture and commercialize infigratinib for any and all human prophylactic and therapeutic uses in all cancer indications (including in combination with other therapies) in certain territories outside the United States. Under the QED-LianBio License Agreement, QED received a nonrefundable upfront payment of $10.0 million and is entitled to receive development and sales milestones payments of up to $132.5 million and tiered royalties on net sales ranging from the low to mid-teens. In addition, QED also received warrants which entitled QED to purchase 10% of the then-fully diluted shares of one of the subsidiaries of LianBio upon achievement of certain contingent development milestones (see Note 7).

We accounted for the QED-LianBio License Agreement and the LianBio Exclusivity Agreement as a single transaction under ASC 606 and identified the exclusive license as a distinct performance obligation since LianBio can benefit from the license on its own by developing and commercializing the underlying product using its own resources. In addition, we will enter into clinical and commercial supply agreements for the licensed territory. We determined that the LianBio's optional right to future products under these supply agreements is not considered to represent a material right. A clinical supply agreement was entered into in the fourth quarter of 2021. QED has supplied insignificant amounts to LianBio as part of the clinical supply agreement and recognized such amounts as license revenue during the year ended December 31, 2021. No such clinical supply was provided to LianBio during the year ended December 31, 2022.

We consider the future potential development milestone as well as the sales-based royalties to be variable consideration. The future potential milestone payments were not included in the transaction price as they were all determined to be fully constrained under ASC 606. We determined that the achievements of such development milestones are contingent upon success in future clinical trials and regulatory approvals, which are not within our control and are uncertain at this stage. We expect that the royalty arrangements and sales-based milestones will be recognized when the sales occur, or the milestones are achieved pursuant to the sales-based royalty exception under ASC 606 because the license is the predominant item to which the royalties or sales-based milestones relate. We will re-evaluate the transaction price at each reporting period and as uncertain events are resolved or other changes in circumstances occur.

License Agreement with Alexion

In September 2019, Eidos, entered into an exclusive license agreement with Alexion Pharma International Operations Unlimited Company, a subsidiary of Alexion Pharmaceuticals, Inc., or together Alexion, to develop, manufacture, and commercialize in Japan the compound known as acoramidis (previously known as AG10) and any of its various chemical forms and any pharmaceutical products containing acoramidis, or the Eidos-Alexion License Agreement. Under the agreement, Eidos received an upfront nonrefundable payment of $25.0 million.

Eidos also entered into a stock purchase agreement with Alexion, under which Eidos sold to Alexion 556,173 shares of Eidos common stock at a price per share of $44.95, for an aggregate purchase price of approximately $25.0 million. The excess of the purchase price over the value of the Eidos shares, determined based on the closing price of a share of Eidos' common stock of $41.91 as reported on Nasdaq as of the date of execution, was $1.7 million and recognized in revenue as part of the upfront payment as discussed below.

Eidos is also eligible to receive $30.0 million in regulatory milestone payments subject to the achievement of regulatory milestones. Eidos will also receive royalty payments in the low-teens based on net sales of acoramidis in Japan. The royalty rate is subject to reduction if Alexion is required to obtain intellectual property rights from third parties to develop, manufacture or commercialize acoramidis in Japan, or upon the introduction of generic competition into market.

Eidos accounted for the license agreement under ASC 606 and identified the exclusive license as a distinct performance obligation since Alexion can benefit from the license on its own by developing and commercializing the underlying product using its own resources. In addition, Eidos entered into a clinical supply agreement and will enter into a commercial supply agreement for the licensed territory. Eidos determined that the optional right to future products under these supply agreements is not considered to represent a material right. Eidos recognized the $25.0 million upfront fee and $1.7 million premium paid for Eidos' stock for a total upfront payment of $26.7 million in license revenue upon the effective date of the license agreement in September 2019. Eidos determined that the license was a right to use its intellectual property and as of the effective date, it had provided all necessary information to Alexion to benefit from the license and the license term had begun.

Eidos considers the future potential regulatory milestones of up to approximately $30.0 million and the sales-based royalties to be variable consideration. Eidos excluded the regulatory milestones from the transaction price because it determined such payments to be fully constrained under ASC 606 due to the inherent uncertainty in the achievement of such milestone payments and are highly susceptible to factors outside of Eidos' control. As the sales-based royalties are all related to the license of the intellectual property rights, Eidos will recognize revenue in the period when subsequent sales are made pursuant to the sales-based royalty exception under ASC 606. Eidos will re-evaluate the transaction price in each reporting period and as uncertain events are resolved or other changes in circumstances occur.

Eidos finalized the clinical supply agreement with Alexion in July 2020, which was determined to be a separate performance obligation from the license. Eidos has shipped insignificant amounts to Alexion as part of the clinical supply agreement and recognized such amounts as license revenue.

12. Sale of Nonfinancial Assets

Sale of Priority Review Voucher

In May 2022, we announced that we entered into a definitive agreement to sell our PRV for $110.0 million. We received the PRV in February 2021 under an FDA program intended to encourage the development of treatments for rare pediatric diseases. We were awarded the PRV when our subsidiary, Origin received approval of NULIBRY™. The PRV sale was subject to customary closing conditions and was completed in June 2022 following the expiration of applicable U.S. antitrust clearance requirements. We accounted for this transaction under ASC 610-20, *Gains and Losses from the Derecognition of Nonfinancial Assets*. We received the gross proceeds of $110.0 million during the year ended December 31, 2022 and recognized a gain of $107.9 million, net of transaction costs, for the year ended December 31, 2022.

Asset Purchase Agreement with Sentynl

On March 4, 2022, Origin and Sentynl entered into the Origin-Sentynl APA, pursuant to which Sentynl acquired global rights to NULIBRY, as well as certain specified assets of Origin, and will be responsible for the ongoing development and commercialization of NULIBRY in the United States and developing, manufacturing and commercializing fosdenopterin globally. The transaction closed on March 31, 2022, or the Closing Date. Under terms of the Origin-Sentynl APA, Origin received an upfront payment of $10.0 million upon the Closing Date and is eligible to receive sales milestone payments, as well as tiered royalties in the low single-digits as a percentage of adjusted net sales of products related to the acquired assets. Origin will continue to be responsible for the payment of up to $4.5 million in aggregate payments upon achievement of regulatory-based milestones, including the first pricing approval in an EMA country or EMA major market country, under the Origin-Alexion APA (see Note 8) and under a separate agreement with a third party. As of December 31, 2022, we paid $3.5 million of the regulatory-based milestone payment as the milestone criteria was met.

We accounted for this transaction under ASC 610-20. Upon the Closing Date, we recognized a loss on sale of $6.3 million within “Other income (expense), net” in our consolidated statement of operations for the year ended December 31, 2022. The loss on sale was determined as the difference in the aforementioned upfront payment and the carrying value of the assets purchased by Sentynl of approximately $16.3 million, which comprised mainly of intellectual property rights and related intangible assets and existing inventories as of the Closing Date.

Origin’s sale of the assets covered in the Origin-Sentynl APA was not subject to the limitation on our ability to dispose of assets under the terms of the Loan Agreement (see Note 10).

13. In-licensing Agreements

Stanford License Agreement

In April 2016, Eidos entered into a license agreement with the Board of Trustees of the Leland Stanford Junior University Stanford University, or Stanford University, relating to Eidos' drug discovery and development initiatives. Under this agreement, Eidos has been granted certain worldwide exclusive licenses to make, use, and sell products that are covered by licensed patent rights. In March 2017, Eidos paid a license fee of $10,000, which was recorded as research and development expense during the year ended December 31, 2017, as the acquired assets did not have any alternative future use. Eidos may also be required to make future payments of up to approximately $1.0 million to Stanford University upon achievement of specific intellectual property, clinical and regulatory milestone events, and pay royalties of up to low single-digit percentages on future net sales, if any. In addition, Eidos is obligated to pay Stanford University a percentage of non-royalty revenue received by Eidos from its sublicensees, with the amount owed decreasing annually for three years based on when the applicable sublicense agreement is executed.

Additionally, under the license agreement with Stanford University, we will pay Stanford University a portion of all nonroyalty sublicensing consideration attributable to the sublicense of the licensed compounds. The license agreement states that if this event occurred in the third year, 10% is payable to Stanford University. For the years ended December 31, 2022, 2021 and 2020, the cost of license revenue was not material.

Leidos Biomedical Research License and Cooperative Research and Development Agreements

In March 2017, TheRas entered into a cooperative research and development agreement, or Leidos CRADA, with Leidos Biomedical Research, Inc., or Leidos. In December 2018, TheRas and Leidos entered into a license agreement, or Initial Leidos License, under which TheRas was granted certain worldwide exclusive licenses to use the licensed compounds. The Leidos Agreements are related to TheRas' drug discovery and development initiatives. The Initial Leidos License was terminated in 2021. TheRas and Leidos entered into two subsequent license agreements, or Additional Leidos Licenses, in August 2022; the two Additional Leidos Licenses related to (i) KRAS G12C inhibitor and (ii) P13Ka breaker compounds. The Leidos CRADA, Initial Leidos License, and Additional Leidos Licenses are also referred to herein as the Leidos Agreements. For the years ended December 31, 2022, 2021, and 2020, TheRas recognized research and development expenses of $3.2 million, $2.8 million, and $2.3 million, respectively, in connection with the Leidos Agreements.

Diagnostics Agreement with Foundation Medicine

As discussed in Note 8, QED and FMI entered into a diagnostics agreement relating to QED's drug discovery and development initiatives. For the years ended December 31, 2022, 2021 and 2020, QED recognized research and development expenses of $2.6 million, $4.2 million, and $4.8 million, respectively, in connection with this agreement.

Other License and Collaboration Agreements

In addition to the agreements described above, we have also entered into other license and collaboration agreements with various institutions and business entities on terms similar to those described above, none of which are material individually or in the aggregate.

14. Leases

We have operating leases for our corporate headquarters, office spaces and laboratory facilities. One of our office space leases has a finance lease component representing lessor provided furniture and office equipment. Our finance lease, which is presented as part of "Property and equipment, net" in our consolidated balance sheets, is not material.

Certain leases include renewal options at our election, and we include the renewal options when we are reasonably certain that the renewal option will be exercised. The lease liabilities were measured using a weighted-average discount rate based on the most recent borrowing rate as of the calculation of the respective lease liability, adjusted for the remaining lease term and aggregate amount of the lease.

The components of lease cost are as follows:

	Year Ended December 31,		
	2022	2021	2020
		(in thousands)	
Straight line operating lease costs	$ 5,172	$ 5,611	$ 3,786
Finance lease costs	443	402	9
Variable lease costs	6,142	4,243	832
Total lease costs	$ 11,757	$ 10,256	$ 4,627

Supplemental cash flow information related to leases are as follows:

	December 31,		
	2022	2021	2020
		(in thousands)	
Cash paid for amounts included in the measurement of lease liabilities			
Operating cash flows for operating leases	$ 6,245	$ 6,122	$ 4,169
Operating cash flows for finance lease	423	272	34
Right-of-use assets obtained in exchange of lease obligations			
Operating leases	240	6,380	19,595
Finance lease	—	—	1,726

Supplemental information related to the remaining lease term and discount rate are as follows:

	December 31,	
	2022	2021
Weighted-average remaining lease term (in years)		
Operating leases	5.3	5.6
Finance lease	3.1	4.1
Weighted-average discount rate		
Operating leases	5.96 %	5.58 %
Finance lease	6.62 %	6.62 %

As of December 31, 2022, future minimum lease payments for our noncancelable operating leases are as follows. Future minimum lease payments under our finance lease are not material.

		Amount (in thousands)
Year ending December 31:		
2023	$	4,495
2024		3,971
2025		3,938
2026		1,869
2027		850
Thereafter		3,355
Total future minimum lease payments		18,478
Imputed interest		(2,529)
Total	$	15,949
Reported as of December 31, 2022		
Operating lease liabilities, current portion	$	3,675
Operating lease liabilities, net of current portion		12,274
Total operating lease liabilities	$	15,949

We recognized an impairment loss for certain asset groups estimated using discounted cash flow model (income approach) of $3.3 million included in “Selling, general and administrative” expenses in our consolidated statement of operations for the year ended December 31, 2021. The impairment loss for the year ended December 31, 2021 includes $2.6 million related to operating lease right-of-use assets and $0.7 million related to property and equipment, namely leasehold improvements, office furniture, and equipment that we no longer use. The impairment loss related to operating lease right-of-use assets for the year ended December 31, 2022 is not material.

Manufacturing Agreement

In December 2019, we entered into a manufacturing agreement with a vendor to secure clinical and commercial scale manufacturing capacity for the manufacture of batches of active pharmaceutical ingredients for product candidates of certain subsidiaries of BridgeBio. Unless terminated as allowed within the manufacturing agreement, the agreement would have expired five years from when qualified operations begin. Under the terms of the agreement, we were assigned a dedicated manufacturing suite for certain months in each calendar year for a one-time fee of $10.0 million, which would be applied to the buildout, commissioning, qualification, validation, equipping and exclusive use of the dedicated manufacturing suite.

We recorded a construction-in-progress asset of $10.0 million for the payments directly associated with the dedicated manufacturing suite as these payments are deemed to represent a non-lease component. In 2020, we entered into a supplemental agreement with the vendor for certain upgrades on the dedicated manufacturing suite and for additional equipment of approximately $0.2 million. As of December 31, 2021, the readiness determination phase of the dedicated manufacturing suite was expected to be completed in 2022.

In March 2022, we mutually agreed with the vendor to terminate the manufacturing agreement. The termination agreement was formalized effective May 2022. In accordance with the termination agreement, we paid the $2.0 million remaining payable related to the dedicated manufacturing suite and a termination fee of $1.8 million. For the year ended December 31, 2022, we recorded an impairment loss of $10.2 million for the carrying value of the construction-in-progress asset that was no longer recoverable as our rights to the dedicated manufacturing suite ceased pursuant to the termination agreement. The aforementioned impairment loss and the termination fee are included as part of “Restructuring, impairment and related charges” in our consolidated statement of operations for the year ended December 31, 2022 (see Note 17).

15. Share Repurchase Program and Shelf Registration

2021 Share Repurchase Program

In May 2021, our Board of Directors authorized and approved a stock repurchase program pursuant to which we may purchase up to $150.0 million of BridgeBio's outstanding common stock. Stock repurchases under the program may be made from time to time, in the open market, in privately negotiated transactions and otherwise, at the discretion of our management and in accordance with applicable federal securities laws, including Rule 10b-18 of the Securities Exchange Act, of 1934, as amended, and other applicable legal requirements. The timing, pricing, and amounts of these repurchases will depend on a number of factors, including the market price of our common stock and general market and economic conditions. The stock repurchase program does not obligate us to repurchase any dollar amount or number of shares, and the program may be suspended or discontinued at any time. We repurchased 3,017,087 shares in the open market at an average price of $49.72 per share for a total of approximately $150.0 million in 2021. The repurchased shares are held in treasury as treasury stock as of December 31, 2022 and 2021.

2020 Shelf Registration

On July 7, 2020, we filed a shelf registration statement on Form S-3, or the 2020 Shelf, with the SEC in relation to the registration of common stock, preferred stock, debt securities, warrants and units or any combination thereof. We also simultaneously entered into an Open Market Sale Agreement with Jefferies LLC and SVB Leerink LLC, or collectively, the Sales Agents, to provide for the offering, issuance and sale by us of up to an aggregate of $350.0 million of our common stock from time to time in "at-the-market" offerings under the 2020 Shelf and subject to the limitations thereof, or the 2020 Sales Agreement. We will pay to the applicable Sales Agents cash commissions of up to 3.0% of the gross proceeds of sales of common stock under the 2020 Sales Agreement. During the year ended December 31, 2022, the Company sold 455,800 shares through this offering at an average price of $10.90 per share, resulting in net proceeds of $4.9 million. As of December 31, 2022, the Company is still eligible to sell up to $345.0 million of our common stock pursuant to the 2020 Sales Agreement under the 2020 Shelf. We did not issue any shares or receive any proceeds from this offering for the years ended December 31, 2021 and 2020.

16. Stock-Based Compensation

Under each of the legal entity's equity plans, we recorded stock-based compensation in the following expense categories in our consolidated statements of operations for employees and non-employees:

	Year Ended December 31, 2022		
	BridgeBio Equity Plan	Other Subsidiaries Equity Plan	Total
		(in thousands)	
Research and development	$ 37,700	$ 287	$ 37,987
Selling, general and administrative	54,669	—	54,669
Restructuring, impairment and related charges	1,172	—	1,172
Total stock-based compensation	$ 93,541	$ 287	$ 93,828

	Year Ended December 31, 2021		
	BridgeBio Equity Plan	Other Subsidiaries Equity Plan	Total
		(in thousands)	
Research and development	$ 53,829	$ 2,366	$ 56,195
Selling, general and administrative	46,357	3,022	49,379
Total stock-based compensation	$ 100,186	$ 5,388	$ 105,574

	Year Ended December 31, 2020			
	BridgeBio Equity Plan	Eidos Equity Plan	Other Subsidiaries Equity Plan	Total
	(in thousands)			
Research and development	$ 16,316	$ 5,743	$ 626	$ 22,685
Selling, general and administrative	30,285	5,159	330	35,774
Total stock-based compensation	$ 46,601	$ 10,902	$ 956	$ 58,459

We have recorded $2.2 million, $6.0 million, and $3.0 million of stock-based compensation expense for the years ended December 31, 2022, 2021, and 2020, respectively, for performance-based milestone awards that were achieved during the period and were settled in cash.

Equity-Based Awards of BridgeBio

On June 22, 2019, we adopted the 2019 Stock Option and Incentive Plan, or the 2019 Plan, which became effective on June 25, 2019. The 2019 Plan provides for the grant of stock-based incentive awards, including common stock options and other stock-based awards. We were authorized to issue 11,500,000 shares of common stock for issuance of awards under the 2019 Plan, which may be allocated among stock options, awards of restricted common stock, restricted common units and other stock-based awards. On June 2, 2020, our stockholders approved an amendment and restatement of the 2019 Plan, or the A&R 2019 Plan, to, among other things, increase the number of shares of common stock reserved for issuance thereunder by 2,500,000 shares. The A&R 2019 Plan was further amended on December 15, 2021, or as amended, the “2021 A&R Plan.

The 2019 Plan provides that the number of shares reserved and available for issuance will automatically increase each January 1, beginning on January 1, 2020, by 5% of the issued and outstanding number of shares of common stock on the immediately preceding December 31, or such lesser number of shares as determined by the Compensation Committee of the Board of Directors.

On November 13, 2019, we adopted the 2019 Inducement Equity Plan, or the 2019 Inducement Plan. The 2019 Inducement Plan provides for the grant of stock-based awards to induce highly qualified prospective officers and employees who are not currently employed by BridgeBio or its Subsidiaries to accept employment and to provide them with a proprietary interest in BridgeBio, including common stock options and other stock-based awards. We were authorized to issue 1,000,000 shares of common stock for inducement awards under the 2019 Inducement Plan, which may be allocated among stock options, awards of restricted common stock, restricted common units and other stock-based awards.

As of December 31, 2022, 7,926,630 shares and 305,588 shares were reserved for future issuances under the 2021 A&R Plan and 2019 Inducement Plan, respectively. Pursuant to the Merger Transactions, we also reserved 2,802,644 shares specifically under the Eidos Award Exchange, or the Eidos Award Exchange Plan, all of which were issued upon execution of the Eidos Award Exchange as discussed below. The 2021 A&R Plan and the 2019 Inducement Plan and the Eidos Award Exchange Plan are collectively referred herein as the “Plans.”

2020 Stock and Equity Award Exchange Program (Exchange Program)

On April 22, 2020, we completed our 2020 Stock and Equity Award Exchange Program, or the Exchange Program, for certain subsidiaries, which was an opportunity for eligible controlled entities' employees and consultants to exchange their subsidiary equity (including common stock, vested and unvested stock options and restricted stock awards, or RSAs) for BridgeBio equity (including common stock, vested and unvested stock options and RSAs) and/or performance-based milestone awards tied to the achievement of certain development and regulatory milestones. The Exchange Program aligns our incentive compensation structure for employees and consultants across the BridgeBio group of companies to be consistent with the achievement of our overall corporate goals. In connection with the Exchange Program, we issued awards of BridgeBio equity under the 2019 A&R Plan to 149 grantees covering 554,064 shares of common stock, 1,268,110 stock options to purchase common stock, 50,145 shares of RSAs and 22,611 shares of performance-based RSAs. The exchange also included performance-based milestone awards of up to $183.4 million to be settled in fully-vested RSAs in the future upon achievement of the milestones, or, collectively, the New Awards. In consideration for all the subsidiaries' shares tendered, BridgeBio increased its ownership in controlled entities included in the Exchange Program and the corresponding noncontrolling interest decreased.

On November 18, 2020, we completed a stock and equity award under our Exchange Program for a subsidiary. We issued awards of BridgeBio equity under the 2019 A&R Plan to 16 grantees covering 24,924 shares of common stock, 70,436 stock options to purchase common stock, and 10,772 shares of performance-based stock options to purchase common stock. The exchange also included performance-based milestone awards of up to $11.7 million to be settled in fully-vested RSAs in the future upon achievement of the milestones.

We evaluated the exchange of the controlled entities' outstanding common stock and equity awards for BridgeBio awards as a modification under ASC 718, *Share Based Payments*. Under ASC 718, a modification is a change in the terms or conditions of a stock-based compensation award. In assessing the accounting treatment, we consider the fair value, vesting conditions and classification as an equity or liability award of the controlled entity equity before the exchange, compared to the BridgeBio equity received as part of the exchange to determine whether modification accounting must be applied. When applying modification accounting, we considered the type of modification to determine the appropriate stock-based compensation cost to be recognized on April 22 and November 18, 2020, (each the "Modification Date"), and subsequent to the Modification Date.

We considered the total shares of common stock and equity awards, whether vested or unvested, held by each participant in each controlled entity as the unit of account. The controlled entity's common stock and equity awards in each unit of account was exchanged for a combination of BridgeBio's common stock, time-based vesting equity awards and/or performance-based milestone awards. Other than the exchange of the controlled entity equity awards for performance-based milestone awards, all other exchanged BridgeBio equity awards retained the original vesting conditions. As a result, there was no incremental stock-based compensation expense resulting from the exchange of time-based equity awards.

At the completion of the Exchange Program, we determined $17.4 million of the performance-based milestone awards were probable of achievement and represented the incremental stock-based compensation cost resulting from the modification of time-based equity awards to performance-based milestone awards. These performance-based milestone awards were to be recognized over a period ranging from 0.7 year to 1.7 years. There was no incremental stock-based compensation cost arising from the completion of the Exchange Program on November 18, 2020. Under ASC 718, we account for such performance-based milestone awards as a liability in "Accrued compensation and benefits" and in "Other long-term liabilities" in the consolidated balance sheets due to the fixed milestone amount that will be converted into a variable number of shares of BridgeBio common stock to be granted upon the achievement date.

For the years ended December 31, 2022, 2021, and 2020, we recognized $0.7 million, $26.7 million and $9.6 million, respectively, of stock-based compensation cost associated with performance-based milestone awards whereby the milestones were determined to be probable of achievement as of each of the reporting date. Refer to Note 9 for contingent compensation accrued associated with performance-based milestones that are determined to be probable as of December 31, 2022.

Performance-based Milestone Awards

Apart from the Exchange Program discussed above, we have performance-based milestone compensation arrangements with certain employees and consultants whose vesting is contingent upon meeting various regulatory and development milestones, with fixed monetary amounts known at inception that can be settled in the form of cash or equity at our sole discretion, upon achievement of each contingent milestone. Upon achievement of a contingent milestone and if such performance-based milestone awards are settled in the form of equity, these are satisfied in the form of fully-vested RSAs. We recognize such contingent stock-based compensation expense when the milestone is probable of achievement. For the years ended December 31, 2022 and 2021 we recognized $1.9 million and $7.9 million, respectively, of stock-based compensation expense associated with performance-based milestone awards that were determined to be probable of achievement as of each reporting date. Refer to Note 9 for contingent compensation accrued associated with performance-based milestones awards that are determined to be probable as of December 31, 2022.

Stock Option Grants of BridgeBio

The following table summarizes BridgeBio's stock option activity under the Plans for the year ended December 31, 2022:

	Options Outstanding		Weighted-Average Exercise Price per Option	Weighted-Average Remaining Contractual Life (years)	Aggregate Intrinsic Value (in thousands)
Outstanding as of December 31, 2021		12,141,756			
Regular equity program	9,493,258		$ 31.85	8.5	$ —
Eidos Awards Exchange	2,107,626		$ 16.14	6.9	$ 10,147
Exchange Program	540,872		$ 2.46	7.0	$ 7,956
Granted		1,468,894			
Regular equity program	1,468,894		$ 8.45		
Exercised		(289,165)			
Eidos Awards Exchange	(155,635)		$ 2.64		
Exchange Program	(133,530)		$ 1.89		
Cancelled		(1,683,624)			
Regular equity program	(1,150,216)		$ 34.80		
Eidos Awards Exchange	(506,106)		$ 23.66		
Exchange Program	(27,302)		$ 6.67		
Outstanding as of December 31, 2022		11,637,861			
Regular equity program	9,811,936		$ 28.00	7.7	$ —
Eidos Awards Exchange	1,445,885		$ 14.96	5.9	$ 1,427
Exchange Program	380,040		$ 2.35	6.2	$ 2,246
Exercisable as of December 31, 2022		7,091,695			
Regular equity program	5,500,728		$ 27.74	7.0	$ —
Eidos Awards Exchange	1,220,199		$ 13.50	5.7	$ 1,418
Exchange Program	370,768		$ 2.24	6.2	$ 2,211

The options granted to employees and non-employees are exercisable at the price of BridgeBio's common stock at the respective grant dates. The options granted have a service condition and generally vest over a period of four years.

The weighted-average grant date fair value of options granted during the year ended December 31, 2022 was $5.24.

The aggregate intrinsic value of options outstanding and exercisable as of December 31, 2022, in the table above are calculated based on the difference between the exercise price and the current fair value of BridgeBio common stock. The total intrinsic value of options exercised during the year ended December 31, 2022, was $2.2 million.

For the years ended December 31, 2022, 2021, and 2020, we recognized stock-based compensation expense of $39.7 million, $31.1 million and $15.6 million, respectively, related to stock options under the Plans. As of December 31, 2022, there was $53.2 million of total unrecognized compensation cost related to stock options under the Plans that is expected to be recognized over a weighted-average period of 2.0 years.

Restricted Stock Units (RSUs) of BridgeBio

The following table summarizes BridgeBio's RSU activity under the Plans for the year ended December 31, 2022:

	Unvested Shares of RSUs Outstanding	Weighted-Average Grant Date Fair Value
Balance as of December 31, 2021	3,537,719	$ 45.36
Granted	4,700,333	$ 8.56
Vested	(1,953,772)	$ 22.42
Cancelled	(2,175,638)	$ 31.32
Balance as of December 31, 2022	4,108,642	$ 21.60

The RSUs have a service condition and generally vest over a period of two to four years.

For the years ended December 31, 2022, 2021, and 2020, we recognized stock-based compensation expense of $43.1 million, $25.0 million, and $7.4 million, respectively, related to shares of RSUs under the Plans. As of December 31, 2022, there was $82.1 million of total unrecognized compensation cost related to RSUs under the Plans that is expected to be recognized over a weighted-average period of 2.2 years.

Restricted Stock Awards (RSAs) of BridgeBio

In 2019, all unvested outstanding management incentive units and common units of BBP LLC which existed prior to the reorganization and IPO were cancelled and converted into shares of BridgeBio's RSAs.

The following table summarizes our RSA activity under the Plans for the year ended December 31, 2022:

	Unvested Shares of RSAs Outstanding	Weighted-Average Grant Date Fair Value
Balance as of December 31, 2021	1,789,943	$ 5.50
Granted — Exchange Program	407,786	$ 7.94
Vested — Exchange Program	(407,786)	$ 7.94
Vested — Regular equity program	(1,091,320)	$ 4.39
Cancelled — Regular equity program	(46,565)	$ 6.22
Balance as of December 31, 2022	652,058	$ 7.29

For the years ended December 31, 2022, 2021 and 2020, we recognized stock-based compensation expense related to RSAs under the Plans as follows:

	Year Ended December 31,		
	2022	2021	2020
		(in thousands)	
Exchange Program	$ 3,238	$ 24,065	$ 2,292
Other RSAs	5,326	6,240	8,384
Total stock-based compensation expense	$ 8,564	$ 30,305	$ 10,676

As of December 31, 2022, there was $4.7 million of total unrecognized compensation cost related to RSAs under the Plans that is expected to be recognized over a weighted-average period of 1.1 year. The respective balances of unvested RSAs as of December 31, 2022 and 2021 are included as outstanding shares disclosed in the consolidated balance sheets as the shares were actually issued but are subject to forfeiture per the terms of the awards.

2019 Employee Stock Purchase Plan (ESPP) of BridgeBio

On June 22, 2019, we adopted the 2019 ESPP, which became effective on June 25, 2019 and was amended and restated effective as of December 12, 2019. The ESPP initially reserves and authorizes the issuance of up to a total of 2,000,000 shares of common stock to participating employees. The ESPP provides that the number of shares reserved and available for issuance will automatically increase each January 1, beginning on January 1, 2020, by the lower of: i) 1% of the outstanding number of shares of common stock on the immediately preceding December 31, ii) 2,000,000 shares or iii) such lesser number of shares as determined by the Compensation Committee.

Under the ESPP, eligible employees may purchase shares of BridgeBio common stock through payroll deductions at a price equal to 85% of the lower of the fair market values of the stock as of the beginning or the end of six-month offering periods. An employee's payroll deductions under the ESPP are limited to 15% of the employee's compensation and employees may not purchase more than 3,500 of shares of BridgeBio common stock during any offering period.

For the year ended December 31, 2022, we recognized $2.6 million of stock-based compensation expense related to our ESPP while the stock-based compensation expense for the years ended December 31, 2021 and 2020 was not material. As of December 31, 2022, 3,895,891 shares were reserved for future issuance under the ESPP.

Valuation Assumptions

We used the Black-Scholes model to estimate the fair value of stock options and stock purchase rights under ESPP. We used the following weighted-average assumptions in the Black-Scholes calculations:

	Year Ended December 31,					
	2022		2021		2020	
	Stock Options	ESPP	Stock Options	ESPP	Stock Options	ESPP
Expected term (in years)	6.00	0.50	5.50-6.08	0.50	5.00-6.08	0.40-0.65
Expected volatility	65.9 %	52.0% - 191.7%	49.0%-52.0%	47.6%-52.0%	36.3%-46.4%	32.5%-47.6%
Risk-free interest rate	3.2 %	0.1% - 3.1%	0.6%-1.3%	0.1%-0.1%	0.3%-1.5%	0.1%-1.6%
Dividend yield	—	—	—	—	—	—
Weighted-average fair value of stock-based awards granted	$ 5.24	$ 6.29	$ 23.09	$ 18.31	$ 11.29	$ 10.48

Equity Awards of Eidos

Prior to the Merger Transactions, Eidos issued its own equity-based awards under the Eidos 2016 Equity Incentive Plan and the Eidos 2018 Stock Option and Incentive Plan, or collectively, the Eidos Plans. Upon closing of the Merger Transactions, we issued 2,776,672 stock options to purchase common stock of BridgeBio and 25,972 shares of BridgeBio RSUs to 88 employees of Eidos under the Eidos Award Exchange in exchange for their then outstanding common stock options and RSUs under the Eidos Plans, or the Replaced Awards. The awards issued in the Eidos Award Exchange have the same vesting terms and conditions as the Replaced Awards. We evaluated the exchange of the awards as a modification under ASC 718 and recognized no incremental compensation cost from such modification.

Stock-based compensation under the Eidos Plans from January 1, 2021 until the closing of the Merger Transactions was not material. For the year ended December 31, 2020, Eidos recognized stock-based compensation expense of $10.9 million which comprised mainly of expenses related to stock options under the Eidos Plans.

For the year ended December 31, 2020, the fair value of Eidos stock option awards was estimated at the date of grant using a Black-Scholes model with the following assumptions:

	Year Ended December 31, 2020
Expected term (in years)	6.06
Expected volatility	72.1 %
Risk-free interest rate	0.52 %
Dividend yield	—

Eidos likewise issued RSUs under the Eidos Plans and had ESPP program under its 2018 Employee Stock Purchase Plan. For the year ended December 31, 2020 stock-based compensation expense under these equity awards was not material.

17. Restructuring, Impairment and Related Charges

In January 2022, we committed to a restructuring initiative designed to drive operational changes in our business processes, efficiencies and cost savings to advance our corporate strategy and development programs. The restructuring initiative included, among other components, consolidation and rationalization of our facilities, reprioritization of development programs and the reduction in our workforce. During the fiscal year ended December 31, 2022, restructuring, impairment and related charges amounted to $43.8 million consisting primarily of winding down costs, exit and other related costs, impairments and write-offs of long-lived assets, and severance and employee-related costs. We are continuing to evaluate our restructuring initiatives for fiscal year 2023 and we estimate to incur total charges in the range of approximately $6.0 million to $9.0 million. Our estimate of the range of costs is subject to certain assumptions and actual results may differ from those estimates or assumptions. We may also incur additional costs that are not currently foreseeable as we continue to evaluate our restructuring alternatives to drive operational changes in business processes, efficiencies and cost savings.

There were no restructuring initiatives in prior years. Restructuring, impairment and related charges included in our consolidated statement of operations for the year ended December 31, 2022 consisted of the following:

	Year ended December 31, 2022 (in thousands)
Winding down, exit and other related costs	$ 20,739
Long-lived assets impairments and write-offs	12,720
Severance and employee-related costs	10,306
Total	$ 43,765

The following table summarizes the activity related to the restructuring liabilities associated with our restructuring initiatives for the year ended December 31, 2022:

	Year ended December 31, 2022
	(in thousands)
Balance as of December 31, 2021	$ —
Reclassification of final payment obligation related to a manufacturing agreement that was recognized in the prior period (see Note 14)	2,185
Restructuring, impairment and related charges	43,765
Cash payments	(25,232)
Noncash activities	(13,892)
Balance as of December 31, 2022	$ 6,826

Reported as of December 31, 2022	(in thousands)
Accounts payable	$ 896
Accrued compensation and benefits	41
Accrued research and development liabilities	5,889
Total	$ 6,826

18. Income Taxes

The following table presents the components of net loss before income taxes:

	Year ended December 31, 2022	2021	2020
		(in thousands)	
Domestic	$ 485,079	$ 586,478	$ 505,488
Foreign	(427)	(24)	—
Total loss before income taxes	$ 484,652	$ 586,454	$ 505,488

There was no current or deferred income tax expense or benefit (domestic and foreign) for the years ended December 31, 2022, 2021, and 2020.

The following table presents a reconciliation of the statutory federal rate and our effective tax rate:

	Year ended December 31, 2022	2021	2020
Tax at statutory federal rate	21.0 %	21.0 %	21.0 %
Change in valuation allowance	(21.7)	(25.6)	(25.0)
Research and development credits	3.2	3.9	3.3
Stock-based compensation	(1.8)	1.2	1
Other	(0.7)	(0.5)	(0.3)
Effective income tax rate	— %	— %	— %

Significant components of our deferred tax assets and liabilities are as follows:

	December 31, 2022	December 31, 2021
	(in thousands)	
Deferred tax assets:		
Net operating loss carry-forwards	$ 325,830	$ 331,537
Amortization	9,172	9,570
Accruals and reserves	5,261	8,833
Stock-based compensation	16,134	10,233
Tax credits	86,012	67,724
Operating lease liabilities	3,075	3,821
Deferred income from asset sale	2,391	—
Capitalized research and experimental expenditures	77,190	—
Deferred interest expense	13,154	—
Property and equipment	600	—
Other	268	448
Gross deferred tax assets	539,087	432,166
Less valuation allowance	(533,929)	(423,909)
Deferred tax assets, net of valuation allowance	5,158	8,257
Deferred tax liabilities:		
Property and equipment	—	(339)
Operating lease right-of-use assets	(2,001)	(2,844)
Unrealized gains and losses	(3,157)	(5,074)
Deferred tax liabilities	(5,158)	(8,257)
Net deferred tax assets (liabilities)	$ —	$ —

As of December 31, 2022, we have net operating loss carryforwards available to reduce future taxable income, if any, for federal and state income tax purposes of approximately $1.4 billion and $255.4 million, respectively. The federal net operating losses generated prior to 2018 amounting to $37.5 million will begin to expire in 2035, losses generated after 2018 amounting to $1.4 billion will carry over indefinitely and would be subject to an 80% taxable income limitation in the year utilized. State net operating losses will generally begin to expire in 2038.

As of December 31, 2022, we had federal research and development and orphan drug credit carryforwards of $92.7 million, which will expire beginning in 2036 if not utilized. As of December 31, 2022, we have California and other state research and development tax credit carryforwards of $17.2 million. The state research and development tax credits will expire at various dates while the California research and development tax credits will carry over indefinitely.

Beginning in 2022, the 2017 Tax Cuts and Jobs Act amended Section 174 to eliminate current-year deductibility of research and experimentation (R&E) expenditures and software development costs (collectively, R&E expenditures) and instead require taxpayers to charge their R&E expenditures to a capital account amortized over five years (15 years for expenditures attributable to R&E activity performed outside the United States). The Company generates a deferred tax asset for capitalized R&E expenditures for the year ended December 31, 2022 which is fully offset with a valuation allowance.

A valuation allowance is provided for deferred tax assets where the recoverability of the assets is uncertain. The determination to provide a valuation allowance is dependent upon the assessment of whether it is more likely than not that sufficient future taxable income will be generated to utilize the deferred tax assets. Based on the weight of the available evidence, which includes our historical operating losses and forecast of future losses, we provided a valuation allowance against the US Federal and state deferred tax assets resulting from the tax loss and credits carried forward. As a result of the issuance of our 2027 Notes in 2020, it was determined that our existing deferred tax assets do not fully offset the deferred tax liabilities when reviewing the reversals of temporary differences. This resulted in a deferred tax liability of $1.1 million that was recognized for the year ended December 31, 2020. We have derecognized the deferred tax liability on January 1, 2021 upon early adoption of ASU 2020-06, with no impact on the provision for income tax. The valuation allowance increased by $110.0 million, $199.5 million, and $95.5 million for the years ended December 31, 2022, 2021, and 2020, respectively.

Utilization of the net operating loss and credit carryforwards may be subject to a substantial annual limitation due to an ownership change limitation as provided by section 382 of the Internal Revenue Code of 1986, as amended, and similar state provisions. The annual limitation may result in the expiration of net operating losses and credits before utilization. In the event that we had a change of ownership, utilization of the net operating loss and tax credit carryforwards may be restricted.

As of December 31, 2022, we had an immaterial amount of undistributed earnings of our non-U.S. subsidiaries for which we have not provided for non-U.S. withholding taxes and state taxes because such earnings are intended to be reinvested indefinitely in international operations. The amount of applicable taxes due if such earnings were distributed would be immaterial. Accordingly, we have not provisioned U.S. state taxes and foreign withholding taxes on non-U.S. subsidiaries for which the earnings are permanently reinvested.

A reconciliation of the beginning and ending amount of unrecognized tax benefits is as follows:

	December 31,	
	2022	2021
	(in thousands)	
Balance at the beginning of the year	$ 21,254	$ 12,524
Additions of prior year positions	724	4,037
Reductions of prior year positions	—	(354)
Additions based on tax positions related to current year	5,035	5,047
Balance at the end of the year	$ 27,013	$ 21,254

As of December 31, 2022 and 2021, we have not recorded interest and penalties associated with our unrecognized tax benefits. Our policy is to recognize interest and penalties related to income tax matters in income tax expense.

Our unrecognized gross tax benefits would not reduce the annual effective tax rate if recognized because we have recorded a valuation allowance on our deferred tax assets.

We file federal and various income tax returns. We currently have no federal or state tax examinations in progress. All years are open for examination by federal and state authorities.

On March 27, 2020, the Coronavirus Aid, Relief, and Economic Security Act, or the CARES Act, was signed into law. The CARES Act includes income tax provisions relating to net operating loss carryback periods, alternative minimum tax credit refunds, modifications to the net interest deduction limitations and technical corrections to tax depreciation methods for qualified improvement property. The CARES Act also allowed for the deferral of employer payroll taxes, which we have done, and the liability is accounted for in our consolidated financial statement. The provisions of the CARES Act did not have a material impact on our consolidated financial statements.

On August 16, 2022, President Biden signed the Inflation Reduction Act of 2022, or the Inflation Act, into law. The Inflation Act contains certain tax measures, including a corporate alternative minimum tax of 15% on some large corporations and an excise tax of 1% on corporate stock buy-backs. The various provisions of the Inflation Act do not have a material impact on the Company's financial statements.

19. Net Loss Per Share Attributable to Common Stockholders of BridgeBio

Basic net loss per share attributable to common stockholders of BridgeBio is computed by dividing net loss attributable to common stockholders of BridgeBio by the weighted-average number of shares of common stock outstanding. Diluted net loss per share attributable to common stockholders of BridgeBio is computed by dividing net loss by the weighted-average number of shares of common stock outstanding, plus all additional common shares that would have been outstanding, assuming dilutive potential common shares had been issued for other dilutive securities. For the years ended December 31, 2022, 2021, and 2020, diluted and basic net loss per share attributable to common stockholders of BridgeBio was identical since potential common shares were excluded from the calculation, as their effect was anti-dilutive.

The following common stock equivalents were excluded from the computation of diluted net loss per share attributable to common stockholders of BridgeBio, because including them would have been antidilutive:

	As of December 31,		
	2022	2021	2020
Unvested RSAs	652,058	1,789,943	3,364,366
Unvested RSUs	4,108,642	3,537,719	1,053,838
Unvested market-based RSUs	—	—	2,380
Unvested performance-based RSUs	7,875	69,340	73,304
Unvested performance-based RSAs	—	—	22,611
Common stock options issued and outstanding	11,637,861	12,141,756	7,632,961
Estimated shares issuable under performance-based milestone compensation arrangements	19,201,212	13,959,588	4,161,970
Estimated shares issuable under the ESPP	217,660	172,927	50,584
Assumed conversion of 2027 Notes	12,878,305	12,878,305	12,878,305
Assumed conversion of 2029 Notes	7,702,988	7,702,988	—
	56,406,601	52,252,566	29,240,319

Our 2029 Notes and 2027 Notes are convertible, based on the applicable conversion rate, into cash, shares of our common stock or a combination thereof, at our election.

As discussed in Notes 9 and 16, we have performance-based milestone compensation arrangements, whose vesting is contingent upon meeting various regulatory and development milestones, with fixed monetary amounts known at inception that can be settled in the form of cash or equity at our sole election, upon achievement of each contingent milestone. The common stock equivalents of such arrangements were estimated as if the contingent milestones were achieved as of the reporting date and the arrangements were all settled in equity.

ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE

Not applicable.

ITEM 9A. CONTROLS AND PROCEDURES

Evaluation of Disclosure Controls and Procedures

We maintain disclosure controls and procedures that are designed to ensure that information required to be disclosed in our periodic and current reports that we file under the Exchange Act of 1934, as amended, with the U.S. Securities and Exchange Commission, or the SEC, is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms, and that such information is accumulated and communicated to our management, including our chief executive officer and principal financial officer, as appropriate, to allow timely decisions regarding required disclosure.

Our management, with the participation of our Chief Executive Officer and our Chief Financial Officer (our principal executive officer and principal financial officer, respectively), evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2022 and concluded that our disclosure controls and procedures were effective at the reasonable assurance level as of that date. The term "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act, means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company's management, including its principal executive and principal financial officers, as appropriate to allow timely decisions regarding required disclosure. Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

Changes in Internal Control over Financial Reporting

There was no change in our internal control over financial reporting identified in connection with the evaluation required by Rule 13a-15(d) and 15d-15(d) of the Exchange Act that occurred during the period covered by this Quarterly Report on Form 10-Q that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Management's Annual Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as defined in Exchange Act Rules 13a-15(f). Our internal control over financial reporting is a process designed under the supervision of our Chief Executive Officer and Chief Financial Officer to provide reasonable assurance regarding the reliability of financial reporting and the preparation of our financial statements for external purposes in accordance with U.S. generally accepted accounting principles.

As of December 31, 2022, we assessed the effectiveness of our internal control over financial reporting based on the criteria for effective internal control over financial reporting under the 2013 "Internal Control — Integrated Framework," issued by the Committee of Sponsoring Organizations, or COSO, of the Treadway Commission, under the supervision of, and with the participation of our management, including our Chief Executive Officer and Chief Financial Officer. Based on that assessment, our management concluded that we maintained effective internal control over financial reporting as of December 31, 2022.

Deloitte & Touche LLP, an independent registered public accounting firm, audited the effectiveness of our internal control over financial reporting as of December 31, 2022, as stated in their attestation report, which is included herein.

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Shareholders and the Board of Directors of BridgeBio Pharma, Inc.

Opinion on Internal Control over Financial Reporting

We have audited the internal control over financial reporting of BridgeBio Pharma, Inc., its subsidiaries and controlled entities (the "Company") as of December 31, 2022, based on criteria established in *Internal Control —Integrated Framework (2013)* issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO). In our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2022, based on criteria established in *Internal Control — Integrated Framework (2013)* issued by COSO.

We have also audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the consolidated financial statements as of and for the year ended December 31, 2022, of the Company and our report dated February 23, 2023, expressed an unqualified opinion on those financial statements.

Basis for Opinion

The Company's management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting. Our responsibility is to express an opinion on the Company's internal control over financial reporting based on our audit. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the US federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audit in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects. Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, testing and evaluating the design and operating effectiveness of internal control based on the assessed risk, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

Definition and Limitations of Internal Control over Financial Reporting

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with accounting principles generally accepted in the United States of America ("generally accepted accounting principles"). A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions or that the degree of compliance with the policies or procedures may deteriorate.

/s/ Deloitte & Touche LLP

San Francisco, California
February 23, 2023

ITEM 9B. OTHER INFORMATION

None.

ITEM 9C. DISCLOSURE REGARDING FOREIGN JURISDICTIONS THAT PREVENT INSPECTIONS

None.

PART III

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

Except as set forth below, the information required by this Item is incorporated by reference from our definitive proxy statement for our 2023 Annual Meeting of Stockholders to be filed with the SEC within 120 days after the end of our fiscal year ended December 31, 2022.

We have adopted a written code of business conduct and ethics that applies to our directors, officers and employees, including our principal executive officer, principal financial officer, principal accounting officer, controller or persons performing similar functions. A current copy of the code is posted on the Corporate Governance section of our website, located at https://investor.bridgebio.com/static-files/e15fa82d-1c86-4951-96a1-0676f0a6bb3d. If we make any substantive amendments to, or grant any waivers from, the code of business conduct and ethics for our principal executive officer, principal financial officer, principal accounting officer, controller or persons performing similar functions, or any officer or director, we will disclose the nature of such amendment or waiver on our website or in a current report on Form 8-K.

ITEM 11. EXECUTIVE COMPENSATION

The information required by this Item is incorporated by reference from our definitive proxy statement for our 2023 Annual Meeting of Stockholders to be filed with the SEC within 120 days after the end of our fiscal year ended December 31, 2022.

ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS

The information required by this Item is incorporated by reference from our definitive proxy statement for our 2023 Annual Meeting of Stockholders to be filed with the SEC within 120 days after the end of our fiscal year ended December 31, 2022.

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE

The information required by this Item is incorporated by reference from our definitive proxy statement for our 2023 Annual Meeting of Stockholders to be filed with the SEC within 120 days after the end of our fiscal year ended December 31, 2022.

ITEM 14. PRINCIPAL ACCOUNTING FEES AND SERVICES

The information required by this Item is incorporated by reference from our definitive proxy statement for our 2023 Annual Meeting of Stockholders to be filed with the SEC within 120 days after the end of our fiscal year ended December 31, 2022.

PART IV

ITEM 15. EXHIBITS AND FINANCIAL STATEMENT SCHEDULES

(a) The following documents are filed as part of this Annual Report on Form 10-K:

1. Financial Statements:

The following financial statements and schedules of the Registrant are contained in Part II, Item 8, "Financial Statements and Supplementary Data" of this Annual Report on Form 10-K:

2. Financial Statement Schedules:

All schedules have been omitted because of the absence of conditions under which they are required or because the required information, where material, is shown in the financial statements, financial notes or supplementary financial information.

(b) Exhibits required by Item 601 of Regulation S-K:

The exhibits listed in the accompanying Exhibit Index are filed as part of, or incorporated by reference into, this Annual Report on Form 10 K.

ITEM 16. FORM 10-K SUMMARY

None.

Exhibits

Exhibit Number	Exhibit Title	Form	File No.	Exhibit	Filing Date
2.1	Agreement and Plan of Merger, dated as of October 5, 2020, by and among BridgeBio Pharma, Inc., Eidos Therapeutic, Inc., Globe Merger Sub I, Inc. and Globe Merger Sub II, Inc. (incorporated by reference to Exhibit 2.1 to BridgeBio's Current Report on Form 8-K filed with the SEC on October 6, 2020).	8-K	001-38959	2.1	January 26, 2021
3.1	Amended and Restated Certificate of Incorporation of the Registrant, as currently in effect.	8-K	001-38959	3.1	July 3, 2019
3.2	Amended and Restated Bylaws of the Registrant, as currently in effect.	S-4	333-249944	3.2	November 6, 2020
4.1	Specimen Common Stock Certificate.	S-1	333-231759	4.1	June 24, 2019
4.2	Form of Registration Rights Agreement, among the Registrant and certain of its shareholders, dated June 26, 2019.	S-1	333-231759	4.3	June 24, 2019
4.3	Description of Securities.	10-K	001-38959	4.3	February 25, 2022
4.4	Indenture, dated as of March 9, 2020, by and between BridgeBio Pharma, Inc. and U.S. Bank National Association, as Trustee.	8-K	001-38959	4.1	March 10, 2020
4.5	Form of Global Note, representing BridgeBio Pharma, Inc.'s 2.50% Convertible Senior Notes due 2027 (included as Exhibit A to the Indenture filed as Exhibit 4.1).	8-K	001-38959	4.2	March 10, 2020
4.6	Indenture, dated as of January 28, 2021, by and between BridgeBio Pharma, Inc. and U.S. Bank National Association, as Trustee.	8-K	001-38959	4.1	January 29, 2021
4.7	Form of Global Note, representing BridgeBio Pharma, Inc.'s 2.25% Convertible Senior Notes due 2029 (included as Exhibit A to the Indenture filed as Exhibit 4.1).	8-K	001-38959	4.2	January 29, 2021
10.1#	Amended and Restated 2021 Stock Option and Incentive Plan and forms of award agreements thereunder.	10-K	001-38959	10.1	February 25, 2022
10.2#	Amended and Restated 2019 Employee Stock Purchase Plan.	10-Q	001-38959	10.1	November 4, 2021

10.3#	Senior Executive Cash Incentive Bonus Plan.	S-1	333-231759	10.3	June 24, 2019
10.4#	Form of Indemnification Agreement, between the Registrant and each of its directors.	S-1	333-231759	10.4	June 24, 2019
10.5#	Form of Indemnification Agreement, between the Registrant and each of its executive officers.	S-1	333-231759	10.5	June 24, 2019
10.6	Lease Agreement, between BridgeBio Pharma LLC and Michael J. Harbour, dated as of March 23, 2017.	S-1	333-231759	10.8	May 24, 2019
10.7	Exclusive (Equity) Agreement, by and between Eidos Therapeutics, Inc. and the Board of Trustees of the Leland Stanford Junior University, effective as of April 10, 2016, as amended by Amendment No. 1 effective September 25, 2017.	S-1	333-231759	10.9	May 24, 2019
10.8	License Agreement, between QED Therapeutics, Inc. and Novartis International Pharmaceutical Ltd., dated as of January 29, 2018.	S-1	333-231759	10.10	May 24, 2019
10.9†	Asset Purchase Agreement, among BridgeBio Pharma LLC, Origin Biosciences, Inc., and Alexion Pharma Holding Unlimited Company, dated as of June 7, 2018.	S-1	333-231759	10.11	May 24, 2019
10.10†	Exclusive Patent License Agreement, between The Frederick National Laboratory for Cancer Research, operated by Leidos Biomedical Research, Inc., under sponsorship from the National Cancer Institute, and TheRas, Inc., dated December 14, 2018.	S-1	333-231759	10.16	May 24, 2019
10.11†	Cell Line License Agreement, by and between Life Technologies Corporation and BridgeBio Services, Inc., effective as of November 15, 2018.	S-1	333-231759	10.17	May 24, 2019
10.12#	Offer Letter, between BridgeBio Services, Inc. and Neil Kumar, dated December 14, 2017.	S-1	333-231759	10.19	June 11, 2019
10.13#	Offer Letter, between BridgeBio Services, Inc. and Brian Stephenson, dated October 28, 2018.	S-1	333-231759	10.20	June 11, 2019
10.14#	Offer Letter, between BridgeBio Services, Inc. and Charles Homcy, dated February 20, 2019.	S-1	333-231759	10.22	June 11, 2019
10.15#	Offer Letter, between BridgeBio Services, Inc. and Richard Scheller, dated April 5, 2019.	S-1	333-231759	10.23	June 11, 2019

10.16#†	Consulting Agreement between Frank McCormick and the Registrant, effective as of January 1, 2021.	—	—	—	Filed herewith
10.17#†	Amendment No. 1 to Consulting Agreement between Frank McCormick and the Registrant, effective as of March 3, 2022.	—	—	—	Filed herewith
10.18#†	Amendment No. 2 to Consulting Agreement between Frank McCormick and the Registrant, effective as of March 3, 2023.	—	—	—	Filed herewith
10.19	Form of Tax Sharing Agreement, between the Registrant and each of its subsidiaries.	S-1	333-231759	10.27	June 24, 2019
10.20	Indemnification Agreement, between BridgeBio Pharma LLC and KKR Genetic Disorder, L.P., dated March 26, 2016.	S-1	333-231759	10.28	June 24, 2019
10.21†	License Agreement, by and between Eidos Therapeutics, Inc. and Alexion Pharma International Operations Unlimited Company, dated September 9, 2019.	10-Q	000-38959	10.1	November 8, 2019
10.22#	BridgeBio Pharma, Inc. 2019 Inducement Equity Plan.	S-8	333-234803	99.1	November 20, 2019
10.23#	Form of Restricted Stock Award Agreement under BridgeBio Pharma, Inc. 2019 Inducement Equity Plan.	S-8	333-234803	99.2	November 20, 2019
10.24#	Form of Non-Qualified Stock Option Agreement under BridgeBio Pharma, Inc. 2019 Inducement Equity Plan.	S-8	333-234803	99.3	November 20, 2019
10.25#	Form of Restricted Stock Unit Award Agreement under BridgeBio Pharma, Inc. 2019 Inducement Equity Plan.	S-8	333-234803	99.4	November 20, 2019
10.26#	Amended and Restated Director Compensation Policy.	10-K	001-38959	10.30	February 25, 2022
10.27	Open Market Sale Agreement[SM], dated as of July 7, 2020.	S-3	333-239734	1.2	July 7, 2020
10.28	Form of Confirmation for Capped Call Transactions.	8-K	001-38959	10.1	March 10, 2020
10.29	Purchase Agreement, dated January 25, 2021, by and among BridgeBio Pharma, Inc. and J.P. Morgan Securities LLC and Mizuho Securities USA LLC, as representatives of the several Initial Purchasers.	8-K	001-38959	10.1	January 26, 2021

10.30	Form of Confirmation for Capped Call Transactions.	8-K	001-38959	10.1	January 29, 2021
10.31†	Loan and Security Agreement, among U.S. Bank National Association in its capacity as Administrative Agent and Collateral Agent, the Lenders party thereto, the Registrant, and certain subsidiaries of the Registrant, dated as of November 17, 2021.	10-K	001-38959	10.39	February 25, 2022
10.32†	First Amendment to the Loan and Security Agreement, among U.S. Bank Trust Company National Association, a successor to U.S. Bank National Association, in its capacity as Administrative Agent and Collateral Agent, the Lenders party thereto, the Registrant, and certain subsidiaries of the Registrant, dated as of May 12, 2022.	10-Q	001-38959	10.2	August 4, 2022
10.33†	Second Amendment to the Loan and Security Agreement, among U.S. Bank Trust Company National Association, a successor to U.S. Bank National Association, in its capacity as Administrative Agent and Collateral Agent, the Lenders party thereto, the Registrant, and certain subsidiaries of the Registrant, dated as of November 30, 2022.	—	—	—	Filed herewith
10.34†	License, Development and Commercialization Agreement, dated May 11, 2022, by and among the Registrant, Navire Pharma, Inc. and Bristol-Myers Squibb Company.	10-Q	001-38959	10.1	August 4, 2022
21	List of Subsidiaries of the Registrant.	—	—	—	Filed herewith
23.1	Consent of Independent Registered Public Accounting Firm.	—	—	—	Filed herewith
24	Power of Attorney (reference is made to signature page hereto).	—	—	—	Filed herewith
31.1	Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.	—	—	—	Filed herewith

31.2	Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.	—	—	—	Filed herewith
32.1*	Certification of Principal Executive Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.	—	—	—	Filed herewith
32.2*	Certification of Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.	—	—	—	Filed herewith
101.INS	Inline XBRL Instance Document.	—	—	—	Filed herewith
101.SCH	Inline XBRL Taxonomy Extension Schema Document.	—	—	—	Filed herewith
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document.	—	—	—	Filed herewith
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document.	—	—	—	Filed herewith
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document.	—	—	—	Filed herewith
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document.	—	—	—	Filed herewith
104	Cover Page Interactive Data File (formatted as inline XBRL with applicable taxonomy extension information contained in Exhibits 101).	—	—	—	Filed herewith

* This certification is deemed to accompany this Annual Report on Form 10-K and will not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liability of that section. Such certification will not be deemed to be incorporated by reference into any filing under the Securities Act of 1933, as amended, or the Exchange Act, except to the extent specifically incorporated by reference into such filing.

# Indicates a management contract or any compensatory plan, contract or arrangement.

† Certain confidential portions (indicated by brackets and asterisks) have been omitted from this exhibit in accordance with the rules of the Securities and Exchange Commission because such information (i) is not material and (ii) is the type that the Registrant treats as private or confidential.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the Registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

BridgeBio Pharma, Inc.

Date: February 23, 2023

By: /s/ Neil Kumar

Neil Kumar, Ph.D.
Chief Executive Officer, Director
(Principal Executive Officer)

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Neil Kumar and Brian Stephenson, as their true and lawful attorney-in-fact and agent, with full power of substitution and resubstitution, for such person and in his or her name, place and stead, in any and all capacities, to sign any and all amendments to the Annual Report on Form 10-K, and to file the same, with all exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorney-in-fact and agent full power and authority to do and perform each and every act and thing requisite and necessary to be done in and about the premises, as fully to all intents and purposes as he or she could do in person, hereby ratifying and confirming all that said attorney-in-fact and agent, or his substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

Signature	Title	Date
/s/ Neil Kumar Neil Kumar, Ph.D.	President, Chief Executive Officer and Director (Principal Executive Officer)	February 23, 2023
/s/ Brian Stephenson Brian Stephenson, Ph.D., CFA	Chief Financial Officer (Principal Financial Officer and Principal Accounting Officer)	February 23, 2023
/s/ Eric Aguiar Eric Aguiar, M.D.	Director	February 23, 2023
/s/ Jennifer E. Cook Jennifer E. Cook	Director	February 23, 2023
/s/ Douglas A. Dachille Douglas A. Dachille	Director	February 23, 2023
/s/ Ronald J. Daniels Ronald J. Daniels	Director	February 23, 2023
/s/ Andrea John Ellis Andrea John Ellis	Director	February 23, 2023
/s/ Fred Hassan Fred Hassan	Director	February 23, 2023

/s/ Charles Homcy Charles Homcy	Director	February 23, 2023
/s/ Andrew W. Lo Andrew W. Lo, Ph.D.	Director	February 23, 2023
/s/ Frank P. McCormick Frank P McCormick	Director	February 23, 2023
/s/ James C. Momtazee James C. Momtazee	Director	February 23, 2023
/s/ Ali Satvat Ali Satvat	Director	February 23, 2023
/s/ Brenton L. Saunders Brenton L. Saunders	Director	February 23, 2023
/s/ Randal Scott Randal Scott, Ph.D.	Director	February 23, 2023
/s/ Hannah Valantine Hannah Valantine, M.D.	Director	February 23, 2023

[***] Certain information in this document has been omitted from this exhibit because it is both (i) not material and (ii) is the type that the Registrant treats as private or confidential.

Exhibit 10.16

CONSULTING AGREEMENT

This Consulting Agreement (the "Agreement") is effective as of January 1, 2021 (the "Effective Date"), and is made by and between Frank McCormick ("Consultant"), an individual located at [***] ("Company"), a Delaware corporation located at 421 Kipling Street, Palo Alto, California 94301, on behalf of itself and its Affiliates (as defined below), each a "Party" and collectively the "Parties." The Parties hereby agree as follows.

1. Services; Payment; No Violation of Rights or Obligations. Consultant agrees to undertake and complete the services as set forth in Exhibit A in accordance with and on the schedule specified in Exhibit A (the "Services"). As the only consideration due Consultant regarding the subject matter of this Agreement, Company will pay Consultant in accordance with Exhibit A. Company may engage Consultant for future services hereunder by entering into mutually executed subsequent exhibits in substantially the same form as Exhibit A. The Parties acknowledge and agree that the fees to be paid to the Consultant hereunder represent the Parties' good faith determination of the fair market value of the Services. Unless otherwise specifically agreed upon by Company in writing (and notwithstanding any other provision of this Agreement), all activity relating to the Services will be performed by and only by Consultant or by employees of Consultant who have been approved in writing in advance by Company with respect to each such employee. Consultant agrees that it will not (and will not permit others to) (a) violate any agreement with or rights of any third party, or (b) except as expressly authorized by Company in writing hereafter, use or disclose at any time Consultant's own or any third party's confidential information or intellectual property, whether in connection with the Services or otherwise, for or on behalf of Company.

2. Confidential Information; Affiliates. As used herein, Company's "Confidential Information" shall mean any and all technical and non-technical information, whether tangible or intangible, disclosed or provided by or on behalf of Company and/or one or more of its Affiliates in written, oral or electronic form in connection with this Agreement, any future discussions about potential engagements, and all Proprietary Information (as defined below). Confidential Information will be deemed to include, without limitation any technology, inventions, patent filings not yet public, products, chemical compounds and compositions, formulations, molecules, precursors, methods, concepts, ideas, plans, processes, specifications, characteristics, techniques, know-how and assays; clinical information such as raw data, scientific preclinical or clinical data, regulatory dossiers, observations, records, databases, dosing regimens, clinical studies or protocols, posters, presentations and abstracts, product pipelines, timelines and schedules; business information such as development, marketing, sales, pricing and commercialization plans, forecasts, proposals, customer lists, suppliers, consulting relationships, operating, performance and cost structures, and any other non-public information, whether

scientific, clinical or financial in nature, relating directly or indirectly to the business of Company; any material that is or has been prepared by or for the Consultant and that contains, reflects, interprets or is based directly or indirectly upon any Confidential Information provided by or on behalf of Company and/or one or more of its Affiliates the existence and terms of this Agreement, and the fact that Confidential Information has been made available to Consultant. For purposes of this Agreement, "Affiliate" shall mean a person or business entity that directly or indirectly controls or is controlled by, or is under common control with, Company. The term "control," including the terms "controlled by" or "under common control with," means the possession of, directly or indirectly, the capability to control the direction of the management and policies through the ownership of voting securities. For the avoidance of doubt, Company and its majority- and wholly-owned subsidiaries are Affiliates of Company and of one another.

3. Ownership Rights; Proprietary Information; Publicity.

a. Company recognizes that as of the Effective Date, Consultant is a member of the faculty of UCSF and may become a member of other institutions or associations in the future (the "Institutions"), and that Consultant's activities are and will be subject to the policies and regulations of the Institutions (the "Applicable Policies"). Consultant has provided Company with a copy of all Applicable Policies that Consultant is subject to, including Exhibit B attached hereto, and will promptly inform Company in writing of any changes or additions to the Applicable Policies and Consultant's affiliated Institutions. If any of the Applicable Policies will in Company's judgment and sole discretion interfere with Consultant's performance of the Services or the rights granted Company hereunder, Company may terminate this Agreement immediately.

Company shall own all right, title and interest (including all intellectual property rights of any sort throughout the world) relating to any and all inventions, works of authorship, designs, know how, ideas and information made or conceived or reduced to practice, in whole or in part, by or for or on behalf of Consultant during the term of this Agreement that relate to the subject matter of or arise out of or in connection with the Services or any Proprietary Information (as defined below), except to the extent belonging to an Institution under the Applicable Policies (collectively, "Inventions") and Consultant will promptly disclose and provide all Inventions to Company. Consultant agrees not to perform activities for Company that are: within the course and scope of Consultant's employment with Institution; utilizing any Institution research facilities; or utilizing any gift, grant, or contract research funds received through the Institution.

b. For purposes of the copyright laws of the United States, all Inventions will constitute works made for hire, except to the extent such Inventions cannot by law be works made for hire. Consultant hereby assigns to Company Consultant's right, title and interest in and to such Inventions. Consultant shall assist Company, at Company's expense, to further evidence, record and perfect such assignment, and to perfect, obtain, maintain, enforce and defend any rights assigned. Consultant hereby irrevocably designates and appoints Company as its agents and attorneys-in-fact, coupled with an interest, to act for and on Consultant's behalf to execute and file any document and to do all other lawfully permitted acts to further the foregoing with the same legal force and effect as if executed by Consultant and all other creators or owners of the applicable Invention. Consultant will neither make any use of any funds, space, personnel, facilities, equipment or other resources of any Institution or other third party in performing the Services hereunder nor take any other action that would result in any Institution or other third party owning or having a right in any Inventions.

c. Consultant will not disclose to Company nor induce the Company to use any confidential information or material belonging to any other party.

d. Consultant agrees that all Inventions and all other business, technical and financial information (including, without limitation, the identity of and information relating to customers or employees) developed, learned or obtained by or on behalf of Consultant during the period that Consultant is to be providing the Services that relate to Company or the business or demonstrably anticipated business of Company or in connection with the Services or that are received by or for Company in confidence, constitute "Proprietary Information." During the term of this Agreement and thereafter, Consultant shall hold in confidence and not disclose or, except in performing the Services, use any Confidential Information. However, Consultant shall not be obligated under this paragraph with respect to Confidential Information Consultant can document is or becomes readily publicly available without restriction through no fault of Consultant. Upon termination or as otherwise requested by Company, Consultant will promptly provide to Company all items and copies containing or embodying Confidential Information (including electronic files), except that Consultant may keep its personal copies of its compensation records and this Agreement. Consultant may disclose the Confidential Information of Company to the extent required by a law, regulation, or an order of a court of competent jurisdiction, provided that Consultant promptly provides Company with prior written notice in order to permit Company to prevent such disclosure and/or to seek confidential treatment of such information. Confidential Information that is disclosed pursuant to such legally required disclosure shall remain otherwise subject to the confidentiality and non-use provisions set forth herein. Consultant also recognizes and agrees that Consultant has no expectation of privacy with respect to Company's telecommunications, networking or information processing systems (including, without limitation, stored computer files, email messages and voice messages) and that Consultant's activity, and any files or messages, on or using any of those systems may be monitored at any time without notice.

e. As additional protection for Confidential Information, Consultant agrees that during the Term (as defined below) (i) and for one (1) year thereafter, Consultant will not directly or indirectly encourage or solicit any employee or consultant of Company to leave Company for any reason and (ii) Consultant will not engage in any activity that is in any way competitive with the business or demonstrably anticipated business of Company, and Consultant will not assist any other person or organization in competing or in preparing to compete with any business or demonstrably anticipated business of Company. Without limiting the foregoing, Consultant may perform services for other persons, provided that such services do not represent a conflict of interest or a breach of Consultant's obligation under this Agreement or otherwise.

f. To the extent allowed by law, Section 3(0) and any license granted Company hereunder includes all rights of paternity, integrity, disclosure and withdrawal and any other rights that may be known as or referred to as "moral rights," "artist's rights," "droit moral," or the like (collectively "Moral Rights"). Furthermore, Consultant agrees that notwithstanding any rights of publicity, privacy or otherwise (whether or not statutory) anywhere in the world, and without any further compensation, Company may and is hereby authorized to (and to allow others to) use Consultant's name in connection with promotion of its business, products or services. To the extent any of the foregoing is ineffective under applicable law, Consultant hereby provides any and all ratifications and consents necessary to accomplish the purposes of the foregoing to the extent possible and agrees not to assert any Moral Rights with respect thereto. Consultant will confirm any such ratifications and consents from time to time as requested by Company. If any other person is in any way involved in any Services, Consultant will obtain the foregoing ratifications, consents and authorizations from such person for Company's exclusive benefit.

g. If any part of the Services or Inventions or information provided hereunder is based on, incorporates, or is an improvement or derivative of, or cannot be reasonably and fully made, used, sold, offered for sale, imported, copied, displayed, performed, reproduced, distributed, used to create derivative works or and otherwise exploited without using or violating technology or intellectual property rights owned by or licensed to Consultant (or any person involved in the Services) and not assigned hereunder, Consultant hereby grants Company and its successors a perpetual, irrevocable, worldwide royalty-free, non-exclusive, sublicensable (through multiple tiers) right and license to exploit and exercise all such technology and intellectual property rights in support of Company's exercise or exploitation of the Services, Inventions, other work or information performed or provided hereunder, or any assigned rights (including any modifications, improvements and derivatives of any of them).

h. Consultant agrees not to file any patent, copyright, trademark or other application or registration based on Company's Confidential Information, and not to seek to make or protect improvements thereon, without Company's prior written approval.

4. Warranties and Other Obligations. Consultant represents, warrants and covenants that: (i) the Services will be performed in a professional and workmanlike manner and that none of such Services nor any part of this Agreement is or will be inconsistent with any obligation Consultant may have to others, including without limitation under the Applicable Policies; (ii) all work under this Agreement shall be Consultant's original work and none of the Services or Inventions nor any development, use, production, distribution or exploitation thereof will infringe, misappropriate or violate any intellectual property or other right of any person or entity (including, without limitation, Consultant); (iii) Consultant has the full right to allow it to provide Company with the assignments and rights provided for herein (and has written enforceable agreements with all persons necessary to give it the rights to do the foregoing and otherwise fully perform this Agreement); (iv) Consultant shall comply with all applicable laws and Company safety rules in the course of performing the Services; (v) if Consultant's work requires a license, Consultant has obtained that license and the license is in full force and effect; (vi) Consultant has disclosed to the Institutions all aspects of Consultant's relationship with the Company that are required to be disclosed under the Applicable Policies, and that Consultant has obtained any required consents or approvals of the Institutions concerning such relationship and this Agreement; (vii) Consultant acknowledges that Company may be obligated to report fees paid to Consultant under this Agreement in accordance with applicable Laws that require reporting of payments or transfers of value provided to health care providers, including, but not limited to, the Physician Payments Sunshine Law, 42 U.S.C. § 13207h, and applicable state sunshine reporting Laws; (viii) Consultant is not debarred pursuant to the Generic Drug Enforcement Act of 1992, 21 U.S.C. §335a, as amended, or any similar applicable law or regulation or excluded by the Office of Inspector General pursuant to 42 U.S.C. §1320a-7, et seq. or any state agency from participation in any federal or state health care program, nor is Consultant under investigation or otherwise

aware of any circumstances which may result in Consultant being debarred or excluded. During the Term (as defined below) and for a period of three (3) years thereafter, Consultant shall immediately notify Company in writing, pursuant to the Notice provisions provided herein, of any change in the status of any representation, warranty, or certification set forth in this Section; and (ix) Consultant shall treat all information relating to an identified or identifiable natural person ("Protected Data") as confidential in accordance with all applicable laws, including without limitation (i) the Health Information Portability and Accountability Act of 1996, as amended from time to time, and any regulation and official guidelines (as amended from time to time) promulgated under that Act ("HIPAA") and (ii) Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, and repealing Directive 95/46/EC ("GDPR"), as appropriate.

5. Term and Termination. This Agreement commences as of the Effective Date and shall continue thereafter for three (3) years (the "Term"), unless otherwise terminated in accordance herewith. If either party breaches a material provision of this Agreement, the other party may terminate this Agreement upon ten (10) days' notice, unless the breach is cured within the notice period. Company also may terminate this Agreement at any time, with or without cause, upon thirty (30) days' notice, but, if (and only if) such termination is without cause, Company shall upon such termination pay Consultant all unpaid, undisputed amounts due for the Services completed prior to the effective date of such termination. Sections 2 (subject to the limitations set forth in Section 3(3.d)) through 9 of this Agreement and any remedies for breach of this Agreement shall survive any termination or expiration. Company may communicate the obligations contained in this Agreement to any other (or potential) client or employer of Consultant.

6. Relationship of the Parties; Independent Contractor; No Employee Benefits. Notwithstanding any provision hereof, Consultant is an independent contractor and is not an employee, agent, partner or joint venturer of Company and shall not bind nor attempt to bind Company in any way. Consultant shall accept any directions issued by Company pertaining to the goals to be attained and the results to be achieved by Consultant, but Consultant shall be solely responsible for the manner and hours in which the Services are performed under this Agreement. Consultant shall not be eligible to participate in any of Company's employee benefit plans, fringe benefit programs, group insurance arrangements or similar programs. Company shall not provide workers' compensation, disability insurance, Social Security or unemployment compensation coverage or any other statutory benefit to Consultant. Consultant shall comply at Consultant's expense with all applicable provisions of workers' compensation laws, unemployment compensation laws, federal Social Security law, the Fair Labor Standards Act, federal, state and local income tax laws, and all other applicable federal, state and local laws, regulations and codes relating to terms and conditions of employment required to be fulfilled by employers or independent contractors. Consultant will ensure that its approved employees, contractors and others involved in the Services, if any, are bound in writing to the foregoing, and to all of Consultant's obligations under any provision of this Agreement, for Company's benefit and Consultant will be responsible for any noncompliance by them. Consultant agrees to indemnify Company from any and all claims, damages, liability, settlement, attorneys' fees and expenses, as incurred, on account of the foregoing or any breach of this Agreement or any other action or inaction by or for or on behalf of Consultant.

7. Assignment. This Agreement and the Services are personal to Consultant and Consultant shall not have the right or ability to assign, transfer or subcontract any rights or obligations under this Agreement without the written consent of Company. Any attempt to do so shall be void. Company may fully assign and transfer this Agreement in whole or part. This Agreement shall be binding upon the Parties and their respective successors and permitted assigns.

8. Notice. All notices under this Agreement shall be in writing and shall be deemed given when personally delivered, or three (3) days after being sent by prepaid certified or registered U.S. mail to the address of the party to be noticed as set forth herein or to such other address as such party last provided to the other by written notice.

9. Miscellaneous. Any breach of Section 2 or 4 will cause irreparable harm to Company for which damages would not be an adequate remedy, and therefore, Company will be entitled to injunctive relief with respect thereto in addition to any other remedies. The failure of either party to enforce its rights under this Agreement at any time for any period shall not be construed as a waiver of such rights. No changes or modifications or waivers to this Agreement will be effective unless in writing and signed by both Parties. In the event that any provision of this Agreement shall be determined to be illegal or unenforceable, that provision will be limited or eliminated to the minimum extent necessary so that this Agreement shall otherwise remain in full force and effect and enforceable. This Agreement shall be governed by and construed in accordance with the laws of the State of California without regard to the conflicts of laws provisions thereof. In any action or proceeding to enforce rights under this Agreement, the prevailing party will be entitled to recover costs and attorneys' fees. Headings herein are for convenience of reference only and shall in no way affect interpretation of the Agreement. This Agreement, together with the Exhibits hereto constitutes the entire agreement between the Parties as to the subject matter hereof, and supersedes any previous oral or written communications, representations, understandings, or agreements between them as to such subject matter. The Parties may execute this Agreement in counterparts, each of which is deemed an original, but all of which together constitute one and the same agreement. Electronic and PDF signatures hereon are legal, valid and enforceable as originals.

10. Defend Trade Secrets Act of 2016; Other Notices. Consultant understands that pursuant to the federal Defend Trade Secrets Act of 2016, Consultant shall not be held criminally or civilly liable under any federal or state trade secret law for the disclosure of a trade secret that (A) is made (i) in confidence to a federal, state, or local government official, either directly or indirectly, or to an attorney; and (ii) solely for the purpose of reporting or investigating a suspected violation of law; or (B) is made in a complaint or other document filed in a lawsuit or other proceeding, if such filing is made under seal. Consultant further understands that nothing contained in this Agreement limits Consultant's ability to (A) communicate with any federal, state or local governmental agency or commission, including to provide documents or other information, without notice to the Company, or (B) share compensation information concerning Consultant or others, except that this does not permit Consultant to disclose compensation information concerning others that Consultant obtains because Consultant's job responsibilities require or allow access to such information.

11. Significant Noncompliance Reporting. For purposes of this Section, "Significant Noncompliance" means a deviation or series of deviations from a Company protocol,

Good Clinical Practices formulated by the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use, regulatory, and/or legal requirements that is likely to affect to a significant degree the safety or rights of a subject participating in a Company-sponsored trial; the stability, quality and/or control of a Company investigational product; or the quality or integrity of the data generated in a Company- sponsored clinical trial. Consultant shall notify the undersigned within one (1) business day of become aware of any suspicion or discovery of Significant Noncompliance.

ACCEPTED AND AGREED TO:

BridgeBio Pharma, Inc.	Frank McCormick
By: /s/ Neil Kumar	/s/ Frank McCormick
Name: Neil Kumar	Date: March 3, 2021
Title: Founder / CEO	
Date: March 4, 2021	

EXHIBIT A

1. **Services**. Consultant shall provide consulting services to the Company generally in the area of oncology and pipeline development matters.

2. **Fees and Payment Terms**. Company shall pay Consultant an annual rate of $500,000.00 for the Services, payable on the 1st of each calendar year. For 2021, the annual rate will be pro-rated at $433,333.33.

3. **Reimbursable Expenses**. So long as Company's prior written approval has been obtained, Consultant shall be entitled to be reimbursed for any reasonable, out-of-pocket travel, lodging and incidental travel expenses incurred in performing the Services, as evidenced by a valid receipt.

EXHIBIT B

UNIVERSITY OF CALIFORNIA STATE OATH OF ALLEGIANCE. PATENT POLICY, AND PATENT ACKNOWLEDGMENT

[***] Certain information in this document has been omitted from this exhibit because it is both (i) not material and (ii) is the type that the Registrant treats as private or confidential.

Exhibit 10.17

AMENDMENT No. 1 TO CONSULTING AGREEMENT

THIS AMENDMENT No. 1 TO CONSULTING AGREEMENT ("**Amendment No. 1**") is effective as of March 3, 2022 (hereinafter "**Effective Date**") by and between BridgeBio Pharma, Inc. (hereinafter "**Company**"), a Delaware corporation with offices at 421 Kipling Street, Palo Alto, California 94301, and Frank McCormick (hereinafter "**Consultant**"), located at [***] (each herein referred to as a "**Party**" and collectively as "**Parties**").

WHEREAS, the Parties wish to amend that certain Consulting Agreement (the "**Agreement**") dated March 3, 2021, by and between Company and Consultant to incorporate certain changes to the Services as set forth below.

NOW, THEREFORE, in consideration of the foregoing and the mutual covenants and premises set forth herein and other good and valuable consideration, the receipt and adequacy of which are hereby acknowledged, the Parties agree as follows:

1. Exhibit A to the Agreement is hereby amended and replaced as set forth in Appendix A hereto.

2. Except as expressly modified hereby, the Agreement shall continue in full force according to its terms.

3. Capitalized terms not otherwise defined in this Amendment No. 1 shall have the meaning ascribed to such term in the Agreement.

4. This Amendment No. 1 shall be effective from the Effective Date.

5. This Amendment No. 1 shall inure to the benefit of, and be binding upon, the Parties hereto and their respective heirs, successors, trustees, transferees, and assigns.

6. This Amendment No. 1 may be executed in any number of counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument.

IN WITNESS WHEREOF, the parties hereto, intending to be legally bound hereby, have caused this Amendment No. 1 and any attachments related thereto to be executed and delivered by their proper and duly authorized officers.

Frank McCormick	BridgeBio Pharma, Inc.
/s/ Frank McCormick	/s/ Neil Kumar
Date: 4 March 2022	By: Neil Kumar
	Title: CEO
	Date: 2 March 2022

Appendix A

Services. Consultant shall provide consulting services to the Company generally in the area of oncology and pipeline development matters.

Fees and Payment Terms. For 2022, Company shall pay Consultant a cash fee of $337,500.00. Once this agreement is effective, Consultant shall submit an invoice for the cash portion of the payment of the fee, which will be payable within 30 days of receipt.

Reimbursable Expenses. So long as Company's prior written approval has been obtained, Consultant shall be entitled to be reimbursed for any reasonable, out-of-pocket travel lodging and incidental travel expenses incurred in performing the Services, as evidenced by a valid receipt.

[***] Certain information in this document has been omitted from this exhibit because it is both (i) not material and (ii) is the type that the Registrant treats as private or confidential.

Exhibit 10.18

AMENDMENT No. 2 TO CONSULTING AGREEMENT

THIS AMENDMENT No. 1 TO CONSULTING AGREEMENT ("**Amendment No. 1**") is effective as of March 3, 2023 (hereinafter "**Effective Date**") by and between BridgeBio Pharma, Inc. (hereinafter "**Company**"), a Delaware corporation with offices at 421 Kipling Street, Palo Alto, California 94301, and Frank McCormick (hereinafter "**Consultant**"), located at [***] (each herein referred to as a "**Party**" and collectively as "**Parties**").

WHEREAS, the Parties wish to amend that certain Consulting Agreement (the "**Agreement**") dated March 3, 2021 and amended March 3, 2022, by and between Company and Consultant to incorporate certain changes to the Services as set forth below.

NOW, THEREFORE, in consideration of the foregoing and the mutual covenants and premises set forth herein and other good and valuable consideration, the receipt and adequacy of which are hereby acknowledged, the Parties agree as follows:

1. Exhibit A to the Agreement is hereby amended and replaced as set forth in Appendix A hereto.

2. Except as expressly modified hereby, the Agreement shall continue in full force according to its terms.

3. Capitalized terms not otherwise defined in this Amendment No. 1 shall have the meaning ascribed to such term in the Agreement.

4. This Amendment No. 2 shall be effective from the Effective Date.

5. This Amendment No. 2 shall inure to the benefit of, and be binding upon, the Parties hereto and their respective heirs, successors, trustees, transferees, and assigns.

6. This Amendment No. 2 may be executed in any number of counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument.

IN WITNESS WHEREOF, the parties hereto, intending to be legally bound hereby, have caused this Amendment No. 1 and any attachments related thereto to be executed and delivered by their proper and duly authorized officers.

Frank McCormick	BridgeBio Pharma, Inc.
/s/ Frank McCormick	/s/ Neil Kumar
Date: January 24, 2023	By: Neil Kumar
	Title: CEO
	January 23, 2023

Appendix A

Services. Consultant shall provide consulting services to the Company generally in the area of oncology and pipeline development matters.

Fees and Payment Terms. For 2023, Company shall pay Consultant a cash fee of $500,000.00. Once this agreement is effective, Consultant shall submit an invoice for the payment of the fee, which will be payable within 30 days of receipt.

Reimbursable Expenses. So long as Company's prior written approval has been obtained, Consultant shall be entitled to be reimbursed for any reasonable, out-of-pocket travel lodging and incidental travel expenses incurred in performing the Services, as evidenced by a valid receipt.

SECOND AMENDMENT TO LOAN AND SECURITY AGREEMENT

This SECOND AMENDMENT TO LOAN AND SECURITY AGREEMENT is made and dated as of November 30, 2022 (this "Second Amendment") by and among BRIDGEBIO PHARMA, INC., a Delaware corporation ("Borrower"), each other Person party hereto as a guarantor (each a "Guarantor" and collectively, the "Guarantors"), the several banks and other financial institutions or entities party hereto (individually or collectively, as the context requires, "Lender" or "Lenders") and U.S. Bank Trust Company, National Association, as successor to U.S. Bank National Association, in its capacity as administrative agent for the Lenders (in such capacity, together with its successors in such capacity, "Administrative Agent") and collateral agent for the Secured Parties (in such capacity, together with its successors in such capacity, "Collateral Agent", and together with the Administrative Agent, the "Agents").

RECITALS

WHEREAS, Borrower, the Guarantors, the Lenders, the Administrative Agent and the Collateral Agent, have entered into that certain Loan and Security Agreement dated as of November 17, 2021 (as amended, supplemented or otherwise modified from time to time prior to the date hereof, the "Existing Loan Agreement"; the Existing Loan Agreement as amended by this Second Amendment, the "Loan Agreement");

WHEREAS, Borrower has requested that the Existing Loan Agreement be amended so as to, among other things: (1) permit certain budgeted expenses to be excluded from the definition of "Net Cash Proceeds" on the terms and conditions specified in the Loan Agreement and (2) permanently terminate the Tranche II Commitments in full; and

WHEREAS, each of the Lenders party hereto, constituting all Lenders party to the Existing Loan Agreement, are willing on the terms and subject to the conditions set forth below, to consent to the amendments to the Existing Loan Agreement set forth herein.

NOW, THEREFORE, in consideration of the covenants and agreements contained herein, as well as other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the parties hereto agree as follows:

ARTICLE I
DEFINITIONS

SECTION 1.1 Certain Definitions. Capitalized terms used (including in the preamble and recitals hereto) but not defined herein shall have the meanings assigned to such terms in the Existing Loan Agreement. As used in this Second Amendment:

"Agents" is defined in the preamble hereto.

"Existing Loan Agreement" is defined in the first recital hereto.

"Second Amendment" is defined in the preamble hereto.

"Second Amendment Effective Date" is defined in Article III to this Second Amendment.

ARTICLE II
AMENDMENTS TO EXISTING LOAN AGREEMENT

SECTION 2.1 Amendments to Existing Loan Agreement. Borrower, each Guarantor, each Lender party hereto and the Agents agree that, effective upon the Second Amendment Effective Date, the Existing Loan Agreement is hereby amended as follows:

(a) To delete the stricken text (indicated textually in the same manner as the following example: ~~stricken text~~) and to add the double-underlined text (indicated textually in the same manner as the following example: double-underlined text) as set forth in Exhibit A attached hereto. For the avoidance of doubt, the Existing Credit Agreement is not being restated, replaced or novated, it being agreed that the attachment hereto of the marked copy thereof is being in such form for convenience only.

(b) The aggregate Tranche II Term Commitments are hereby permanently terminated in full pursuant to Section 2.10(c) of the Existing Loan Agreement, and Schedule 1.1 of the Existing Loan Agreement is hereby replaced with Schedule 1.1 attached hereto as Exhibit B. The Lenders party hereto agree to waive any notice requirements specified in the Existing Loan Agreement in respect of such permanent termination of Tranche II Term Commitments in full.

ARTICLE III

CONDITIONS TO EFFECTIVENESS

The effectiveness of this Second Amendment is subject to the satisfaction (or waiver) of the following conditions (the date on which such conditions are satisfied (or waived), the "Second Amendment Effective Date"):

SECTION 3.1 This Second Amendment shall have been duly executed by Borrower, each Guarantor, the Administrative Agent, the Collateral Agent and each of the Lenders, and delivered to the Administrative Agent.

SECTION 3.2 No Default or Event of Default shall exist or would result from the amendments made herein on the Seco Amendment Effective Date.

SECTION 3.3 The representations and warranties of each Loan Party set forth in Section 5 of the Existing Loan Agreement, Article IV of this Second Amendment and in each other Loan Document shall be true and correct in all material respects (or, to the extent any such representation or warranty is qualified by any applicable standard of materiality, in all respects) on and as of the Second Amendment Effective Date with the same effect as though made on and as of such date, except to the extent such representations and warranties expressly relate to an earlier date, in which case they shall be true and correct in all respects as of such earlier date.

SECTION 3.4 Administrative Agent shall have received (A) resolutions of the board of directors or applicable governing body of each Loan Party authorizing the execution, delivery and performance of this Second Amendment, certified by an appropriate officers of each such Loan Party, (B) a certificate of each Loan Party, dated the Second Amendment Effective Date, substantially in the form of the certificate or certificates delivered pursuant to Section 4.1(a)(iii) and Section 4.1(a)(iv) of the Existing Loan Agreement, or confirming that the documents and information certified in such certificates remain true, correct and complete in all respects as so certified; and (C) a certificate with respect to the Budgeted Amount in connection with Navire Prepayment Event (as defined below).

SECTION 3.5 Lenders and the Agents shall have received, to the extent invoiced prior to the Second Amendment Effective Date, reimbursement or payment of all out-of-pocket expenses (including reasonable fees, charges and disbursements of counsel) required to be reimbursed or paid by any Loan Party under any Loan Document.

SECTION 3.6 Borrower and the Guarantors shall have delivered to the Agents and Lenders such documents and other information reasonably requested in writing prior to the Second Amendment Effective Date that the Agents or any Lender has reasonably determined is required by United States regulatory authorities under applicable “know your customer” and anti-money laundering rules and regulations, including without limitation Title III of the USA Patriot Act.

ARTICLE IV
REPRESENTATIONS AND WARRANTIES

SECTION 4.1 Representations and Warranties.

(a) Each Loan Party’s execution, delivery and performance of this Agreement and all other Loan Documents, (i) have been duly authorized by all necessary action in accordance with such Loan Party’s Organizational Documents, (ii) will not result in the creation or imposition of any Lien upon the Collateral, other than Permitted Liens and the Liens created by this Agreement and the other Loan Documents, (iii) do not violate any provisions of (A) such Loan Party’s Organizational Documents, or (B) any, law, regulation, order, injunction, judgment, decree or writ to which such Loan Party is subject and which violation would have a Material Adverse Effect and (iv) do not violate any contract or agreement or require the consent or approval of any other Person which has not already been obtained if such violation or failure to obtain consent or approval would have a Material Adverse Effect. The individual or individuals executing the Loan Documents are duly authorized to do so.

(b) The representations and warranties of each Loan Party set forth in Section 5 of the Existing Loan Agreement, Article IV of this Second Amendment and in each other Loan Document are true and correct in all material respects (or, to the extent any such representation or warranty is qualified by any applicable standard of materiality, in all respects) on and as of the Second Amendment Effective Date with the same effect as though made on and as of such date, except to the extent such representations and warranties expressly relate to an earlier date, in which case they are true and correct in all respects as of such earlier date.

(c) No Default or Event of Default exists or will result from the amendments made herein on the Second Amendment Effective Date.

ARTICLE V
EFFECTS ON LOAN DOCUMENTS

SECTION 5.1 Except as specifically amended herein, all Loan Documents shall continue to be in full force and effect and are hereby in all respects ratified and confirmed.

(a) The execution, delivery and effectiveness of this Second Amendment shall not operate as a waiver of any right, power or remedy of any Lender or Administrative Agent under any of the Loan Documents, nor constitute a waiver of any provision of the Loan Documents or in any way limit, impair or otherwise affect the rights and remedies of the Lenders or the Agents under the Loan Documents. Without limiting the generality of the foregoing, in entering into this Second Amendment, each of the Agents shall be entitled to all of the rights, benefits, privileges, protections, indemnities and immunities afforded to it pursuant to the Loan Documents. By its execution below, each of the Lenders party hereto, constituting all of the Lenders under the Existing Loan Agreement, has consented to the terms of this Second Amendment and hereby directs the Agents to enter into this Second Amendment.

(b) The Borrower and the other parties hereto acknowledge and agree that, on and after the Second Amendment Effective Date, this Second Amendment and each of the other Loan Documents to be executed and delivered by a Loan Party in connection herewith shall constitute a Loan Document for all purposes of the Existing Loan Agreement.

(c) On and after the Second Amendment Effective Date, each reference in the Existing Loan Agreement to "this Agreement", "hereunder", "hereof", "herein" or words of like import referring to the Existing Loan Agreement, and each reference in the other Loan Documents to "Loan Agreement", "thereunder", "thereof" or words of like import referring to the Existing Loan Agreement shall mean and be a reference to the Existing Loan Agreement, as amended by this Second Amendment, and shall be read together and construed as a single instrument.

(d) Nothing herein shall be deemed to entitle the Borrower to a further consent to, or a further waiver, amendment, modification or other change of, any of the terms, conditions, obligations, covenants or agreements contained in the Existing Loan Agreement or any other Loan Document in similar or different circumstances.

(e) Section headings used herein are for convenience of reference only, are not part of this Second Amendment and are not to affect the construction of, or to be taken into consideration in interpreting, this Second Amendment.

(f) Each Lender party hereto and each Loan Party acknowledges and agrees that in connection with that certain License, Development and Commercialization Agreement, dated as of May 11, 2022, by and among Navire Pharma, Inc., Borrower and Bristol-Myers Squibb Company (the Prepayment Event arising therefrom, the "Navire Prepayment Event"), as of the date hereof, the mandatory prepayments made from the proceeds therefrom on or prior to the date hereof by the Borrower satisfy the mandatory prepayment requirements of Section 2.4(b)(i) of the Loan Agreement on or prior to the date hereof with respect to any proceeds received therefrom in all respects. For the avoidance of doubt, in connection with the Navire Prepayment Event, the mandatory prepayment requirements of Section 2.4(b)(i) of the Loan Agreement shall continue to apply to (i) any Net Cash Proceeds received after the date hereof and (ii) and any Overbudgeted Amount with respect thereto.

ARTICLE VI
MISCELLANEOUS

SECTION 6.1 APPLICABLE LAW. THIS SECOND AMENDMENT SHALL BE GOVERNED BY, AND CONSTRUED IN ACCORDANCE WITH, THE LAW OF THE STATE OF NEW YORK (EXCLUDING CONFLICT OF LAWS PRINCIPLES THAT WOULD CAUSE THE APPLICATION OF LAWS OF ANY OTHER JURISDICTION).

SECTION 6.2 Execution in Counterparts; Severability. This Second Amendment may be executed in one or more counterparts, each of which shall be deemed an original, but all of which, when taken together, shall constitute one and the same instrument. Delivery by facsimile transmission or other electronic transmission of an executed counterpart of a signature page of this Second Amendment shall be effective as delivery of an original executed counterpart hereof. The words “execution,” “signed,” “signature,” and words of like import in this Second Amendment and the other Loan Documents shall be deemed to include electronic signatures or electronic records, each of which shall be of the same legal effect, validity or enforceability as a manually executed signature or the use of a paper-based recordkeeping system, as the case may be, to the extent and as provided for in any applicable law, including the Federal Electronic Signatures in Global and National Commerce Act, the New York State Electronic Signatures and Records Act, or any other similar state laws based on the Uniform Electronic Transactions Act.

SECTION 6.3 MUTUAL WAIVER OF JURY TRIAL / JUDICIAL REFERENCE. Section 11.10 of the Existing Loan Agreement is incorporated herein by reference, mutatis mutandis.

SECTION 6.4 Reaffirmation. Each of the Loan Parties party to the Loan Agreement and the other Loan Documents, in each case as amended, supplemented or otherwise modified from time to time, hereby (i) acknowledges and agrees that all of its obligations under the Loan Documents to which it is a party are reaffirmed and remain in full force and effect on a continuous basis, (ii) reaffirms each Lien granted by each Loan Party to Collateral Agent for the benefit of the Secured Parties and reaffirms the guaranties made pursuant to the Existing Loan Agreement, (iii) acknowledges and agrees that the grants of security interests by and the guaranties of the Loan Parties contained in the Existing Loan Agreement and the other Loan Documents (as applicable) are, and shall remain, in full force and effect after giving effect to the Second Amendment, and (iv) agrees that the Secured Obligations include, among other things and without limitation, the prompt and complete payment and performance by the Borrower when due and payable (whether at the stated maturity, by acceleration or otherwise) of principal and interest on, and premium (if any) on, the Loans under the Existing Loan Agreement (as amended by this Second Amendment). Nothing herein contained shall be construed as nor is intended by the parties to be, or shall be, construed as a substitution or novation of the instruments, documents and agreements securing the Secured Obligations, which shall each remain in full force and effect.

ARTICLE VII
WAIVER RELEASE AND DISCLAIMER

SECTION 7.1 IN CONSIDERATION OF, AMONG OTHER THINGS, THE EXECUTION AND DELIVERY OF THIS SECOND AMENDMENT BY THE AGENTS AND EACH LENDER PARTY THAT IS A PARTY HERETO, EACH LOAN PARTY HEREBY IRREVOCABLY FOREVER RELEASES AND DISCHARGES THE LENDERS AND AGENTS AND THEIR AFFILIATES, SUBSIDIARIES, SUCCESSORS, ASSIGNS, DIRECTORS, OFFICERS, EMPLOYEES, AGENTS, CONSULTANTS AND ATTORNEYS (EACH, A “RELEASED PERSON”) OF AND FROM ANY AND ALL CLAIMS, SUITS, ACTIONS, INVESTIGATIONS, PROCEEDINGS OR DEMANDS, WHETHER BASED IN CONTRACT, TORT, IMPLIED OR EXPRESS WARRANTY, STRICT LIABILITY, CRIMINAL OR CIVIL STATUTE OR COMMON LAW OF ANY KIND OR CHARACTER, KNOWN OR UNKNOWN, WHICH SUCH LOAN PARTY EVER HAD OR NOW HAS AGAINST THE AGENTS, ANY OTHER SECURED PARTY OR ANY OTHER RELEASED PERSON WHICH RELATES, DIRECTLY OR INDIRECTLY, TO ANY ACTS OR OMISSIONS OF AGENTS, ANY LENDER PARTY OR ANY OTHER RELEASED PERSON RELATING TO THE EXISTING LOAN AGREEMENT OR ANY OTHER LOAN DOCUMENT ON OR PRIOR TO THE DATE OF EXECUTION OF THIS AMENDMENT. THE PROVISIONS OF THIS SECTION 7.1 SHALL SURVIVE THE TERMINATION OF THIS AMENDMENT, THE LOAN AGREEMENT, THE OTHER LOAN DOCUMENTS, OR PAYMENT IN FULL OF THE SECURED OBLIGATIONS AND THE TERMINATION OF ALL TERM COMMITMENTS.

[Remainder of page intentionally left blank.]

IN WITNESS WHEREOF, the parties hereto have caused this Second Amendment to be duly executed and delivered by their respective proper and duly authorized officers as of the day and year first above written.

BORROWER:

BRIDGEBIO PHARMA, INC.

Signature:	/s/ Neil Kumar
Print Name:	Neil Kumar
Title:	President and Chief Executive Officer

GUARANTORS:

BRIDGEBIO PHARMA LLC

Signature:	/s/ Neil Kumar
Print Name:	Neil Kumar
Title:	President and Chief Executive Officer

BRIDGEBIO SERVICES INC.

Signature:	/s/ Neil Kumar
Print Name:	Neil Kumar
Title:	President and Chief Executive Officer

QED THERAPEUTICS, INC.

Signature:	/s/ Neil Kumar
Print Name:	Neil Kumar
Title:	President

EIDOS THERAPEUTICS, INC.

Signature:	/s/ Neil Kumar
Print Name:	Neil Kumar
Title:	President and Chief Executive Officer

ADRENAS THERAPEUTICS, INC.

Signature:	/s/ Neil Kumar
Print Name:	Neil Kumar
Title:	Treasurer

[Signature Page to Second Amendment]

GUARANTORS (Cont'd):

CALCILYTIX THERAPEUTICS, INC.

Signature:	/s/ Neil Kumar
Print Name:	Neil Kumar
Title:	President

PHOENIX TISSUE REPAIR, INC.

Signature:	/s/ Neil Kumar
Print Name:	Neil Kumar
Title:	President

ORIGIN BIOSCIENCES, INC.

Signature:	/s/ Neil Kumar
Print Name:	Neil Kumar
Title:	President

ML BIO SOLUTIONS INC.

Signature:	/s/ Christine Siu
Print Name:	Christine Siu
Title:	Chief Executive Officer

BRIDGEBIO GENE THERAPY LLC.

Signature:	/s/ Eric David
Print Name:	Eric David
Title:	President

GUARANTORS (Cont'd):

BRIDGEBIO CHEMISTRY, INC.

Signature:	/s/ Neil Kumar
Print Name:	Neil Kumar
Title:	President

[Signature Page to Second Amendment]

ADMINISTRATIVE AGENT:

U.S. BANK TRUST COMPANY, NATIONAL ASSOCIATION, as. successor to U.S. BANK NATIONAL ASSOCIATION

Signature:	/s/ Prital Patel
Print Name:	Prital Patel
Title:	Vice President

COLLATERAL AGENT:

U.S. BANK TRUST COMPANY, NATIONAL ASSOCIATION, as. successor to U.S. BANK NATIONAL ASSOCIATION

Signature:	/s/ John Correia
Print Name:	John Correia
Title:	Vice President

LENDERS:

[***]

Exhibit A

Amended Loan Agreement

[Attached]

[Signature Page to Second Amendment]

EXHIBIT A

LOAN AND SECURITY AGREEMENT

THIS LOAN AND SECURITY AGREEMENT is made and dated as of November 17, 2021 and is entered into by and among BRIDGEBIO PHARMA, INC., a Delaware corporation ("Borrower"), each other Person party hereto from time to time as a guarantor, the several banks and other financial institutions or entities from time to time parties to this Agreement (individually or collectively, as the context requires, "Lender" or "Lenders") and U.S. Bank National Association, in its capacity as administrative agent for the Lenders (in such capacity, together with its successors in such capacity, "Administrative Agent") and collateral agent for the Secured Parties (in such capacity, together with its successors in such capacity, "Collateral Agent").

RECITALS

A. Borrower has requested (after giving effect to the First Amendment **and the Second Amendment**) that Lenders make available to Borrower one or more term loans in an aggregate principal amount of up to $~~550,000,000~~**450,000,000**, in each case subject to the satisfaction or waiver of the relevant conditions to the making of each such Loan, consisting of ~~(i)~~ $450,000,000 in aggregate principal amount of term loans to be funded on the Closing Date as the Tranche I Advance ~~and (ii) up to $100,000,000 in aggregate principal amount of term loans to be made as the Tranche II Advance(s), which such Tranche II Advance(s) shall be made on terms and conditions otherwise identical to the Tranche I Advance~~; and

B. Lenders are willing to make such term loan or term loans on the terms and conditions set forth in this Agreement.

AGREEMENT

NOW, THEREFORE, each Loan Party, Agent and Lender agree as follows:

SECTION 1. DEFINITIONS AND RULES OF CONSTRUCTION

1.1 Unless otherwise defined herein, the following capitalized terms shall have the following meanings:

"Account Control Agreement(s)" means any agreement entered into by and among Agent, any Loan Party and a third party bank or other institution (including a Securities Intermediary) in which such Loan Party maintains a Deposit Account or an account holding Investment Property and which perfects Agent's first priority security interest in the subject account or accounts.

"[***] Milestone Date" [***].

"Acquisition" means any transaction or series of related transactions for the purpose of or resulting, directly or indirectly, in (a) the acquisition of all or substantially all of the assets of a Person, or of any business, line of business or division or other unit of operation of a Person, (b) the acquisition of fifty percent (50%) or more of the Equity Interests of any Person, whether or not involving a merger, consolidation or similar transaction with such other Person, or otherwise causing any Person to become a Subsidiary of any Loan Party, or (c) the acquisition of, or the right to use, develop, license or sell (in each case, including through licensing), any product, product line, royalty rights or Intellectual Property of or from any other Person.

"ADH1" means autosomal dominant hypocalcemia type 1.

"Administrative Agent" has the meaning given to such term in the preamble to this Agreement.

"Advance" or "Advances" means, individually or collectively as the context may require, any Term Loan Advance or the Term Loan Advances.

"Advance Date" means the funding date of any Advance.

"Advance Request" means a request for Advance submitted by Borrower to Administrative Agent in substantially the form of Exhibit A.

"Affected Financial Institution" means (a) any EEA Financial Institution or (b) any UK Financial Institution.

"Affiliate" means any Person that directly or indirectly controls, is controlled by, or is under common control with the Person in question. As used in the definition of "Affiliate," the term "control" means the possession, directly or indirectly, of the power (x) to vote twenty percent (20%) or more of the equity interests having ordinary voting power for the election of directors of such Person or other Persons performing similar functions for any such Person, or (y) to direct or cause the direction of the management and policies of a Person, whether through ownership of voting securities, by contract or otherwise. If not otherwise specified or required by the context, "Affiliate" shall refer to an Affiliate of a Loan Party.

"Agent" means any of Administrative Agent and the Collateral Agent (including their permitted successors and assigns), individually or collectively as the context requires, and "Agents" shall mean any or each Agent collectively, as the context requires.

"Agent Fee Letter" means the fee letter, dated the date of this Agreement, among the Loan Parties and the Agents, as amended, amended and restated, supplemented or otherwise modified from time to time.

"Agreement" means this Loan and Security Agreement, as amended, restated, supplemented or otherwise modified from time to time.

"Anti-Corruption Laws" means all laws, rules, and regulations of any jurisdiction applicable to Borrower or any of its Affiliates from time to time concerning or relating to bribery or corruption, including without limitation the United States Foreign Corrupt Practices Act of 1977, as amended, the UK Bribery Act 2010 and other similar legislation in any other jurisdictions.

"Anti-Terrorism Laws" means any laws, rules, regulations or orders relating to terrorism or money laundering, including without limitation Executive Order No. 13224 (effective September 24, 2001), the USA PATRIOT Act, the laws comprising or implementing the Bank Secrecy Act, and the laws administered by OFAC.

"Applicable Rate" means a per annum rate of interest equal to nine percent (9.00%), of which, at Borrower's election and subject to Section 2.1(c) [***], up to three percent (3.00%) of such per annum rate of interest may be in the form of PIK Interest.

"Article 55 BRRD" means Article 55 of Directive 2014/59/EU establishing a framework for the recovery and resolution of credit institutions and investment firms.

"Assignee" has the meaning given to it in Section 11.13.

"ATTR-CM" means transthyretin amyloid cardiomyopathy.

"Available Investment Amount" means, as of the applicable date of determination, an amount equal to [***].

"Available Investment Period" means the period commencing on January 1 and ending on December 31 of any fiscal year.

"Bail-In Action" means the exercise of any Write-Down and Conversion Powers by the applicable EEA Resolution Authority in respect of any liability of an EEA Financial Institution.

"Bail-In Legislation" means, (a) with respect to any EEA Member Country implementing Article 55 of Directive 2014/59/EU of the European Parliament and of the Council of the European Union, the implementing law for such EEA Member Country from time to time that is described in the EU Bail-In Legislation Schedule and (b) with respect to the United Kingdom, Part I of the United Kingdom Banking Act 2009 (as amended from time to time) and any other law, regulation or rule applicable in the United Kingdom relating to the resolution of unsound or failing banks, investment firms or other financial institutions or their affiliates (other than through liquidation, administration or other insolvency proceedings).

"BB Square Capital" means BB Square GP I, LLC, BB Square LP Investment, LLC, BB Square Capital Partners I, LP, BB Square Holdings, LLC and BB Square Capital, LLC (and their respective successors, assigns and transferees, by acquisitions, Disposition, merger or otherwise).

"BHC Act Affiliate" of a party means an "affiliate" (as such term is defined under, and interpreted in accordance with, 12 U.S.C. § 1841(k)) of such party.

"Blocked Person" means any Person: (a) listed in the annex to, or is otherwise subject to the provisions of, Executive Order No. 13224, (b) a Person owned or controlled by, or acting for or on behalf of, any Person that is listed in the annex to, or is otherwise subject to the provisions of, Executive Order No. 13224, (c) a Person with which any Lender is prohibited from dealing or otherwise engaging in any transaction by any Anti-Terrorism Law, (d) a Person that commits, threatens or conspires to commit or supports "terrorism" as defined in Executive Order No. 13224, or (e) a Person that is named a "specially designated national" or "blocked person" on the most current list published by OFAC or other similar list.

"Board" means, with respect to any Person that is a corporation, its board of directors, with respect to any Person that is a limited liability company, its board of managers, board of members or similar governing body, and with respect to any other Person that is a legal entity, such Person's governing body in accordance with its Organizational Documents.

"Board Approved Projections" has the meaning given to it in Section 7.1(f).

"Borrower" has the meaning given to such term in the preamble to this Agreement.

“Budgeted Amount” means, with respect to any Budgeted Period and without duplication of any amounts included in the “Budgeted Amount” with respect to any other Prepayment Event(s), an amount equal to all operational expenses directly attributable to the performance of obligations by any Platform Company or associated Loan Party pursuant to the definitive agreement related to the applicable Prepayment Event and budgeted for the Budgeted Period in good faith by such Platform Company or Loan Party and payable to third-parties that are not Affiliates of a Loan Party or Platform Company, in each case as certified by the Chief Executive Officer or the Chief Financial Officer of Borrower, including, but not limited to: [***]**. For the avoidance of doubt, “Budgeted Amount” shall not include corporate general and administrative expenses, overhead expenses, or any expenses reimbursed or reimbursable by any third-party that is not an Affiliate of a Loan Party or Platform Company, but may include intercompany charges or expenses (e.g., FTE costs) allocated to Affiliates of a Loan Party or Platform Company in the ordinary course and consistent with past practice and specifically identified in the definitive agreement related to the applicable Prepayment Event.**

“Budgeted Period” means, with respect to any Prepayment Event, the period commencing on the date a definitive agreement governing the transaction underlying such Prepayment Event is executed and ending on the [***] **day thereafter or, with respect to Navire Prepayment Event, ending on** [***]**.**

“Business Day” means any day other than Saturday, Sunday and any other day on which banking institutions in the State of New York or Wilmington, Delaware are closed for business.

“CAH” means congenital adrenal hyperplasia.

“Cash” means all cash and Cash Equivalents.

“Cash Equivalents” has the meaning given to it in clause (b) of the definition of Permitted Investment.

“Cash Management Services” means any of the following to the extent not constituting a line of credit (other than an overnight draft facility that is not in default); automated clearing house transactions, treasury and/or cash management services, including, without limitation, treasury, depository, overdraft, credit, purchasing or debit card, non-card e-payable services, electronic funds transfer, treasury management services (including controlled disbursement services, overdraft automatic clearing house fund transfer services, return items and interstate depository network services), other demand deposit or operating account relationships, foreign exchange facilities, and merchant services.

“CFC” means a Subsidiary that is a “controlled foreign corporation” within the meaning of Section 957 of the Code.

“Change in Control” means a transaction or series of related transactions (i) pursuant to which, or as a result of which, a single Person or group (within the meaning of Section 13(d)(3) of the Exchange Act) acquires or holds equity interests of Borrower representing (A) a majority of the outstanding voting securities (in each case excluding any unvested voting securities that would not become vested voting securities as a result of such transaction, whether pursuant to the terms of such unvested voting securities, by Board action or otherwise), or (B) the right to receive a majority of the proceeds in a final liquidation, dissolution or termination, voluntary or involuntary, of Borrower, or (ii) where a “change of control,” “fundamental change” or any other comparable term under any indenture governing any Permitted Convertible Debt (but not “make-whole fundamental change” unless it results in a put right for holders of such Permitted Convertible Debt) has occurred or a “change of control” or any other comparable term under any Permitted Senior Debt or other Indebtedness for borrowed money with an aggregate principal amount (including undrawn commitments) in excess of $10,000,000 has occurred. Notwithstanding the foregoing, a "Change in Control" shall not include any Permitted Transfer.

"Change in Law" means the occurrence, after the date of this Agreement, of any of the following: (a) the adoption or taking effect of any law, rule, regulation or treaty, (b) any change in any law, rule, regulation or treaty or in the administration, interpretation, implementation or application thereof by any Governmental Authority or (c) the making or issuance of any request, rule, guideline or directive (whether or not having the force of law) by any Governmental Authority.

"Charter" means, with respect to any Person, such Person's formation documents, as in effect from time to time.

"Claims" has the meaning given to it in Section 11.10(a).

"Closing Date" means the first date on which the conditions to make the Tranche I Advance were satisfied or waived in accordance with Section 4 hereof, which date was November 17, 2021.

"Code" means the Internal Revenue Code of 1986, as amended from time to time, and the rules and regulations promulgated thereunder from time to time.

"Collateral" means the property described in Section 3.1. For the avoidance of doubt, "Pledged Collateral" shall be deemed to constitute part of the "Collateral".

"Collateral Agent" has the meaning given to such term in the preamble to this Agreement.

"Compliance Certificate" means a certificate in the form attached hereto as Exhibit F.

"Confidential Information" has the meaning given to it in Section 11.12.

"Contingent Obligation" means, as applied to any Person, any direct or indirect liability, contingent or otherwise, of that Person with respect to (i) any Indebtedness, lease, dividend, letter of credit or other obligation of another, including any such obligation directly or indirectly guaranteed, endorsed, co-made or discounted or sold with recourse by that Person, or in respect of which that Person is otherwise directly or indirectly liable; (ii) any obligations with respect to undrawn letters of credit, corporate credit cards or merchant services issued for the account of that Person; and (iii) all obligations arising under any interest rate, currency or commodity swap agreement, interest rate cap agreement, interest rate collar agreement, or other agreement or arrangement designated to protect a Person against fluctuation in interest rates, currency exchange rates or commodity prices; provided, however, that the term "Contingent Obligation" shall not include endorsements for collection or deposit in the ordinary course of business. The amount of any Contingent Obligation shall be deemed, without duplication of the primary obligation, to be an amount equal to the stated or determined amount of the primary obligation in respect of which such Contingent Obligation is made or, if not stated or determinable, the maximum reasonably anticipated liability in respect thereof as determined by such Person in good faith; provided, however, that such amount shall not in any event exceed the maximum amount of the obligations under the guarantee or other support arrangement. For the avoidance of doubt, no Permitted Bond Hedge Transaction or Permitted Warrant Transaction will be considered a Contingent Obligation of any Loan Party.

“Controlled Account” means a Deposit Account or account in which Investment Property is maintained that is subject to an Account Control Agreement in favor of Collateral Agent in form and substance reasonably satisfactory to Required Lenders and to Collateral Agent, in respect of its rights, duties and obligations.

“Controlled Investment Affiliate” means, as to any Person, any other Person, which directly or indirectly is in control of, is controlled by, or is under common control with such Person.

“Copyright License” means any written agreement granting any right to use any Copyright or Copyright registration, now owned or hereafter acquired by a Loan Party or in which such Loan Party now holds or hereafter acquires any interest.

“Copyrights” means all copyrights, whether published or unpublished, registered or unregistered, now or hereafter existing, created, acquired or held pursuant to the laws of the United States of America, any State thereof, or of any other country.

“Covered Entity” means any of the following:

(a) a “covered entity” as that term is defined in, and interpreted in accordance with, 12 C.F.R. § 252.82(b);

(b) a “covered bank” as that term is defined in, and interpreted in accordance with, 12 C.F.R. § 47.3(b); or

(c) a “covered FSI” as that term is defined in, and interpreted in accordance with, 12 C.F.R. § 382.2(b).

“Debtor Relief Laws” means the Bankruptcy Code of the United States of America, and all other liquidation, conservatorship, bankruptcy, assignment for the benefit of creditors, moratorium, rearrangement, receivership, insolvency, reorganization, or similar debtor relief laws of the United States of America or other applicable jurisdictions from time to time in effect.

“Default” means any event, occurrence or condition which is, or with the giving of any notice, the passage of time, or both, could reasonably be expected to result in an Event of Default.

“Defaulting Lender” means, subject to Section 2.11(b), any Lender that (a) has failed to (i) fund all or any portion of a Loan hereunder within [***] Business Days of the date such Loan was required to be funded hereunder unless such Lender notifies the Agent and Borrower in writing that such failure is the result of such Lender’s determination that one or more conditions precedent to funding (each of which conditions precedent, together with any applicable default, shall be specifically identified in such writing) has not been satisfied, or (ii) pay to the Agent or any other Lender any other amount required to be paid by it hereunder within [***] Business Days of the date when due, (b) has notified Borrower or the Agent in writing that it does not intend to comply with its funding obligations hereunder, or has made a public statement to that effect (unless such writing or public statement relates to such Lender’s obligation to fund a Loan hereunder and states that such position is based on such Lender’s determination that a condition precedent to funding (which condition precedent, together with any applicable default, shall be specifically identified in such writing or public statement) cannot be satisfied), (c) has failed, within [***] Business Days after written request by the Agent or the Borrower to confirm in writing to the Agent and Borrower that it will comply with its prospective funding obligations hereunder (provided that such Lender shall cease to be a Defaulting Lender pursuant to this clause (c) upon receipt of such written confirmation by the Agent or the Borrower), or (d) has, or has a direct or indirect parent company that has, (i) become the subject of a proceeding under any Debtor Relief Law, (ii) had appointed for it a receiver, custodian, conservator, trustee, administrator, assignee for the benefit of creditors or similar Person charged with reorganization or liquidation of its business or assets, including the Federal Deposit Insurance Corporation or any other state or federal regulatory authority acting in such a capacity or (iii) become the subject of a Bail-In Action; provided that a Lender shall not be a Defaulting Lender solely by virtue of the ownership or acquisition of any equity interest in that Lender or any direct or indirect parent company thereof by a Governmental Authority so long as such ownership interest does not result in or provide such Lender with immunity from the jurisdiction of courts within the United States or from the enforcement of judgments or writs of attachment on its assets or permit such Lender (or such Governmental Authority) to reject, repudiate, disavow or disaffirm any contracts or agreements made with such Lender. Any determination by the Agent that a Lender is a Defaulting Lender under any one or more of clauses (a) through (d) above shall be conclusive and binding absent manifest error, and such Lender shall be deemed to be a Defaulting Lender (subject to Section 2.11(b) upon delivery of written notice of such determination to Borrower and each Lender.

"Default Right" has the meaning assigned to that term in, and shall be interpreted in accordance with~~,~~ 12 C.F.R. §§ 252.81, 47.2 or 382.1, as applicable.

"Delaware Divided LLC" means any Delaware LLC which has been formed upon the consummation of a Delaware LLC Division.

"Delaware LLC" means any limited liability company organized or formed under the laws of the State of Delaware.

"Delaware LLC Division" means the statutory division of any Delaware LLC into two or more Delaware LLCs pursuant to Section 18-217 of the Delaware Limited Liability Company Act.

"Delayed Draw Expiration Date" has the meaning given to it in Section 2.1(a)(ii).

"Deposit Accounts" means any "deposit accounts," as such term is defined in the UCC, and includes any checking account, savings account, or certificate of deposit.

"Disposition" means, in respect of any Person, any voluntary or involuntary sale, transfer, lease, license, lending or advancement of funds or assets, conveyance of any equitable, beneficial or legal interest, or other disposition of any property, including any Equity Interest owned by it and including any disposition of property to a Delaware Divided LLC pursuant to a Delaware LLC Division (or any comparable event under a different jurisdiction's laws), or any option for any of the foregoing. "Dispose" shall have a correlative meaning.

"Disqualified Institution" means (a) any of those Persons who are bona fide competitors of Borrower that are identified by Borrower in writing prior to the Closing Date, which list of bona fide competitors of Borrower may be updated by the Borrower on a quarterly basis by sending such updated list to the Agent and the Lenders, provided that any such updates shall not take effect until [***] Business Days after the updated Disqualified Institution list is made available to the Lenders, or (b) any of those banks, financial institutions and other Persons separately identified by Borrower in writing prior to the Closing Date (and, in each case, such specified entities' Affiliates that are reasonably identifiable as Affiliates solely on the basis of their name, provided that the Agent shall have no obligation to carry out due diligence in order to identify such Affiliates). A list of the Disqualified Institutions shall be provided by the Agent to a Lender upon its request, including in connection with an assignment or participation hereunder; provided that, any Person that is a Lender and subsequently becomes a Disqualified Institution (but was not a Disqualified Institution at the time it became a Lender) will be deemed to not be a Disqualified Institution hereunder.

"Domestic Subsidiary" means any Subsidiary of Borrower organized under the laws of the United States, any State thereof or the District of Columbia

"EEA Financial Institution" means (a) any credit institution or investment firm established in any EEA Member Country that is subject to the supervision of an EEA Resolution Authority, (b) any entity established in an EEA Member Country that is a parent of an institution described in clause (a) of this definition, or (c) any financial institution established in an EEA Member Country that is a subsidiary of an institution described in clauses (a) or (b) of this definition and is subject to consolidated supervision with its parent.

"EEA Member Country" means any of the member states of the European Union, Iceland, Liechtenstein, and Norway and any other country which may become a member of the European Economic Area or subject to Bail-In Legislation from time to time.

"EEA Resolution Authority" means any public administrative authority or any person entrusted with public administrative authority of any EEA Member Country (including any delegee) having responsibility for the resolution of any EEA Financial Institution.

"Eidos" means Eidos Therapeutics, Inc.

"Equity Cash Payment Conditions" means, with respect to a given Equity Cash Payment Transaction, in each case measured immediately before and immediately after giving effect to any payments to be made in connection with such Equity Cash Payment Transaction: (a) no Default or Event of Default shall have occurred and be continuing, (b) the Milestone Satisfaction Date has occurred and (c) immediately after giving effect to such Equity Cash Payment Transaction, the Loan Parties shall have Qualified Cash in an amount equal to or greater than (x) [***], in each case as set forth in the Board Approved Projections for the relevant period of determination.

"Equity Cash Payment Transaction" means any transaction or series of related transactions whereby any Cash or other immediately available funds are distributed, exchanged, redeemed, deposited, paid, settled or otherwise transferred for, on account of, or in connection with the ownership of any Equity Interests or other ownership rights in any capital stock, joint venture or similar interests, including without limitation in connection with any Permitted Investments, Permitted Indebtedness or any transaction permitted under Section 7.7 of this Agreement.

"Equity Cure Investment" means any Investment by a Loan Party in a Platform Company or Subsidiary thereof, whether directly or indirectly through an Affiliate or another Platform Company, if (i) immediately prior to the consummation of such Investment, an event of default has occurred and is continuing pursuant to the terms of any secured loan facility to which such Platform Company or Subsidiary is a party, which could result in the acceleration of Indebtedness of such Platform Company in excess of $[***] or more, and (ii) immediately after the making of such Investment, such event of default will be cured or waived.

"Equity Documents" means any agreement entered into in connection with an equity financing or otherwise among holders of the Equity Interests of a Person or otherwise binding upon the holders of the Equity Interests of such Person.

"Equity Interests" means, with respect to any Person, the capital stock, partnership or limited liability company interest, or other equity securities or equity ownership interests of such Person.

"Equity Sale Milestone" means a sale or series of sales (including in connection with business development transactions) of Borrower's common stock for cash by Borrower after the First Amendment Effective Date to third-party purchasers who are not Affiliates of Borrower.

"Equity Sale Premium" means the portion of the proceeds from any Equity Sale Milestone (other than any publicly-marketed follow-on financing, at-the-market offering (including pursuant to that certain Open Market Sale Agreement, dated July 7, 2020, by and among Borrower, Jefferies LLC and SVB Leerink LLC, as may be amended from time to time) or similar publicly marketed transaction), received in connection with any transaction or series of transactions related to any business development, corporate collaboration, private investment in public equity transaction **involving a Disposition or other transaction with respect to the Collateral or any other asset (including Intellectual Property) of a Loan Party (other than the underlying sale of Equity Interests) to the extent constituting a Prepayment Event**, licensing transaction or similar non-publicly marketed transaction, which portion of such proceeds shall be deemed to be equal to (x) the gross cash proceeds received by Borrower from such Equity Sale Milestone *minus* (y) the Equity Sale Proceeds from such Equity Sale Milestone.

"Equity Sale Proceeds" means the proceeds from any Equity Sale Milestone, which proceeds shall be deemed to be (a) with respect to any publicly-marketed follow-on financing, at-the-market offering (including pursuant to that certain Open Market Sale Agreement, dated July 7, 2020, by and among Borrower, Jefferies LLC and SVB Leerink LLC, as may be amended from time to time), or similar publicly marketed transaction, the gross cash proceeds received by Borrower from such Equity Sale Milestone and (b) for all other Equity Sale Milestones, the lesser of (x) the gross cash proceeds received by Borrower from such Equity Sale Milestone and (y) the fair market value of Borrower's common stock sold from such Equity Sale Milestone, as determined by reference to [***].

"ERISA" means the Employee Retirement Income Security Act of 1974, as amended, and the regulations promulgated thereunder.

"EU Bail-In Legislation Schedule" means the EU Bail-In Legislation Schedule published by the Loan Market Association (or any successor person), as in effect from time to time.

"Event of Default" has the meaning given to it in Section 9.

"Exchange Act" means the Securities Exchange Act of 1934, as amended from time to time, and the rules and regulations promulgated pursuant thereto.

"Excluded Accounts" means Deposit Accounts (i) established in the ordinary course of business and used exclusively for payroll, payroll taxes and other employee wage and benefit payments to or for the benefit of employees of the Loan Parties, provided that the aggregate balance maintained in such Deposit Accounts shall not exceed the amount to be paid for the following four payroll periods at any time, (ii) used exclusively as escrow, fiduciary, withholding, tax payment or trust accounts, (iii) used exclusively to maintain Cash subject to a Lien permitted pursuant to the defined term "Permitted Liens" (other than, for the avoidance of doubt, Deposit Accounts subject to control agreements in favor of any Permitted Senior Debt, which will be subject to the terms and conditions of an intercreditor agreement in respect of such Permitted Senior Debt), (iv) that is a deposit account subject to a zero dollar balance, and (v) that do not at any time have Cash, investment property or other amounts on deposit therein in excess of $[***] individually or $[***] in the aggregate for all such accounts, provided that, in each case, any Excluded Account shall be identified to Agent in writing.

"Excluded Taxes" means any of the following Taxes imposed on or with respect to a Recipient or required to be withheld or deducted from a payment to a Recipient: (a) Taxes imposed on or measured by net income (however denominated), franchise Taxes, and branch profits Taxes, in each case, (i) imposed as a result of such Recipient being organized under the laws of, or having its principal office or, in the case of any Lender, its applicable lending office located in, the jurisdiction imposing such Tax (or any political subdivision thereof), or (ii) that are Other Connection Taxes, (b) in the case of a Lender, U.S. federal withholding Taxes that are imposed on amounts payable to or for the account of such Lender with respect to an applicable interest in a Loan or Term Commitment pursuant to a law in effect on the date that (i) such Lender acquires such interest in the Loan or Term Commitment or (ii) such Lender changes its lending office, except in each case to the extent that, pursuant to Section 2.8, amounts with respect to such Taxes were payable either to such Lender's assignor immediately before such Lender became a party hereto or to such Lender immediately before it changed its lending office, (c) any withholding Taxes imposed under FATCA, and (d) Taxes attributable to such Recipient's failure to comply with Section 2.8(d).

"Existing Priority Review Voucher" means that certain Priority Review Voucher (PRV NDA 214018), which voucher was issued by the FDA to Origin on February 28, 2021 and subsequently transferred to [***].

"FATCA" means Sections 1471 through 1474 of the Code, as of the date of this Agreement (or any amended or successor version that is substantively comparable and not materially more onerous to comply with), any current or future regulations or official interpretations thereof, any agreements entered into pursuant to Section 1471(b)(1) of the Code and any fiscal or regulatory legislation, rules or practices adopted pursuant to any intergovernmental agreement, treaty or convention among governmental authorities and implementing such Sections of the Code.

"FDA" means the United States Food and Drug Administration or any successor agency thereto.

"FDA Criteria" means that:

(i) [***]

(ii) [***]

(a) [***]

(b) [***]

(c) [***]

(iii) [***]

"Fee Letter" means that certain Fee Letter, dated as of the date of this Agreement, among the Loan Parties and each Lender, as amended, amended and restated, supplemented or otherwise modified from time to time with the consent of each Lender.

"Fee Letters" means, collectively, the Agent Fee Letter and the Fee Letter.

"First Amendment" means the First Amendment to Loan and Security Agreement, dated as of the First Amendment Effective Date, among Borrower, the Guarantors, the Lenders, the Administrative Agent and the Collateral Agent.

"First Amendment Effective Date" means May 12, 2022.

"Financial Statements" has the meaning given to it in Section 7.1.

"Foreign Lender" shall mean a Lender that is not a U.S. Person.

"Foreign Subsidiary" means any Subsidiary of Borrower that is not a Domestic Subsidiary.

"Foreign Subsidiary Holdco" means any Subsidiary of Borrower that owns no material assets other than Equity Interests (or Equity Interests and Indebtedness) of one or more Foreign Subsidiaries that are CFCs.

"GAAP" means generally accepted accounting principles in the United States of America, as in effect from time to time.

"Governmental Authority" means the government of the United States of America or any other nation, or of any political subdivision thereof, whether state or local, and any agency, authority, instrumentality, regulatory body, court, central bank or other entity exercising executive, legislative, judicial, taxing, regulatory or administrative powers or functions of or pertaining to government (including any supra-national bodies such as the European Union or the European Central Bank).

"Guarantor" means each Subsidiary of Borrower listed as a "Guarantor" on the signature pages hereto and each other Person which guarantees, pursuant to Section 12 or otherwise, all or any part of the Secured Obligations.

"Hedge Agreement" means any interest rate, currency or commodity swap agreement, interest rate cap agreement, interest rate collar agreement, fuel or mineral or other commodity hedge or exchange agreement or any other agreement or arrangement entered into for non-speculative purposes designated to protect a Person against fluctuation in interest rates, currency exchange rates, commodity or mineral prices.

"Hercules Loan Agreement" means that certain Loan and Security Agreement, dated as of June 19, 2018 (as amended, restated, amended and restated, supplemented or otherwise modified from time to time), among Borrower, Hercules Capital, Inc. and the lenders and other parties party thereto.

"Indebtedness" means indebtedness of any kind, including (a) all indebtedness for borrowed money or the deferred purchase price of property or services (excluding trade credit entered into in the ordinary course of business), including reimbursement and other obligations with respect to surety bonds, letters of credit, banker's acceptances and similar instruments, (b) all obligations evidenced by notes, bonds, debentures or similar instruments, (c) all capital lease obligations, as determined under GAAP, (d) guarantees of indebtedness of third parties and (e) all Contingent Obligations. For the avoidance of doubt, no Permitted Warrant Transaction shall be considered Indebtedness of Borrower.

"Indemnified Person" shall have the meaning set forth in Section 6.13.

"Indemnified Taxes" means (a) Taxes, other than Excluded Taxes, imposed on or with respect to any payment made by or on account of any obligation of any Loan Party under any Loan Document and (b) to the extent not otherwise described in clause (a), Other Taxes.

"Intellectual Property" means all of each Loan Party's Copyrights; Trademarks; Patents; Licenses; trade secrets and inventions; mask works; each Loan Party's applications therefor and reissues, extensions, or renewals thereof; and each Loan Party's goodwill associated with any of the foregoing, together with each Loan Party's rights to sue for past, present and future infringement of Intellectual Property and the goodwill associated therewith.

"Intercompany Subordination Agreement" means that certain intercompany subordination agreement, dated as of the Closing Date, by and among the Loan Parties, each Subsidiary and the Agent, substantially in the form attached hereto as Exhibit J, as may be amended, supplemented or otherwise modified from time to time.

"Investment" means, as to any Person, any acquisition or investment, including any beneficial ownership (including stock, partnership or limited liability company interests) of or in any other Person, or any loan (by way of guarantee, Contingent Obligations or otherwise), advance or capital contribution to any other Person or the acquisition of any asset, property or indebtedness of another Person, including by means of (a) the purchase or other acquisition of Equity Interests or debt or other securities of another Person (including in connection with any Acquisition) or (b) a loan, advance or capital contribution to, Guarantee or assumption of Indebtedness of, or purchase or other acquisition of any other debt or equity participation or interest in, another Person, including any partnership or joint venture interest in such other Person (and including, for the avoidance of doubt, any acquisition of or similar investment in any Platform Company).

"Investment Company Act" means the Investment Company Act of 1940, as amended, and the rules and regulations promulgated thereunder.

"Joinder Agreements" means a completed and executed Joinder Agreement in substantially the form attached hereto as Exhibit G.

"Lender" or "Lenders" has the meaning given to each such term in the preamble to this Agreement.

"LGMD2i" means limb-girdle muscular dystrophy type 2I.

"Liabilities" shall have the meaning given to such term in Section 6.3.

"License" means any Copyright License, Patent License, Trademark License or other license of rights or interests.

"Lien" means any mortgage, deed of trust, pledge, hypothecation, assignment for security, security interest, encumbrance, levy, lien or charge of any kind, whether voluntarily incurred or arising by operation of law or otherwise, against any property, any conditional sale or other title retention agreement, and any lease in the nature of a security interest.

"Loan" means the Advances made under this Agreement.

"Loan Documents" means this Agreement, any Term Note (if any), the Fee Letters, the Account Control Agreements, any Joinder Agreements, the Intercompany Subordination Agreement and any other documents executed in connection with the Secured Obligations and the security interest granted in connection therewith, in each case, as the same may from time to time be amended, modified, supplemented or restated.

"Loan Party" means each of Borrower and the Guarantors; "Loan Parties" means Borrower and the Guarantors, collectively.

"Make-Whole Amount" means, on any date of prepayment, repayment or that has become or is declared accelerated pursuant to Section 10.1 or otherwise, or in respect of which such claim in an insolvency proceeding has arisen of all or any portion of the outstanding Advance pursuant to Section 2.4(a), as calculated by Borrower, an amount equal to the net present value of all required interest payments due on the Advance or portion thereof that is being prepaid, repaid or is declared accelerated from the date of prepayment, repayment or acceleration to, but excluding, the first anniversary of the Closing Date (other than, for the avoidance of doubt, accrued but unpaid interest to the date of prepayment), computed using a discount rate equal to the Treasury Rate [***] and assuming (x) that the interest rate applicable to all such interest is the Applicable Rate in effect on the date of such prepayment, (y) all rates are calculated on the basis of a 360-day year consisting of twelve 30-day months and actual days elapsed and (z) all such interest on the Advance or portion thereof being prepaid, repaid or accelerated is paid entirely in cash with no election for PIK Interest. For the avoidance of doubt, such amount shall be payable whether before or after an Event of Default or acceleration of the Loans.

"Market Capitalization" means, as of any date of determination, an amount equal to (a) the summation of the product of (x) the daily volume weighted average price of Borrower's common stock as reported for each trading day during the immediately preceding January 1 through December 31 (it being understood that a "trading day" shall mean a day on which shares of Borrower's common stock trade on the NASDAQ (or other stock exchange, if no longer traded on NASDAQ) in an ordinary trading session) multiplied by (y) the total number of issued and outstanding shares of Borrower's common stock that are issued and outstanding on such trading date and listed on the NASDAQ (or other stock exchange, if no longer traded on NASDAQ), after dividing such summation of values in clauses (a)(x) and (a)(y) by (b) the total number of such trading days in such relevant period of calculation. Such determination shall be appropriately adjusted for any stock dividend, stock split, stock combination, reclassification or other similar transaction during the applicable calculation period. Notwithstanding anything to the contrary herein, the Market Capitalization for the Available Investment Period ending December 31, 2021 for purposes of calculating the Available Investment Amount for relevant usage during the period commencing on the Closing Date and ending on December 31, 2021 shall be equal to $[***].

"Material Adverse Effect" means a material adverse effect upon: (i) the business, operations, properties, assets or financial condition of the Loan Parties and each of its Subsidiaries taken as a whole; or (ii) the ability of the Loan Parties, taken as a whole, to perform or pay the Secured Obligations in accordance with the terms of the Loan Documents, or the ability of Agent or Lenders to enforce any of its rights or remedies with respect to the Secured Obligations; or (iii) the Collateral or Agent's Liens on the Collateral or the priority of such Liens except, in the case of clauses (ii) or (iii), to the extent resulting from an action or failure to act by Agent or Lenders, as applicable.

"Material Intellectual Property" means any Intellectual Property that is material to the business or operations of the Borrower, any Loan Party or any Platform Company, including, but not limited to, (i) Intellectual Property covering or relating to [***] (other than in connection with any Disposition pursuant to clause (h) of the definition of "Permitted Transfers"), and [***], (ii) Intellectual Property covering or relating to the product candidates that are the subject of the clinical trials referenced in the definition of "Other Milestones" and (iii) any other Intellectual Property covering or relating to any product candidates owned or controlled by the Borrower, the Loan Parties or the Platform Companies that become the subject of a Phase 1 Clinical Trial.

"Maturity Date" means November 17, 2026.

"Maximum Rate" has the meaning given to such term in Section 2.2.

"Milestone Approval Date" means [***].

"Milestone Satisfaction Date" [***].

"Navire Prepayment Event" has the meaning given to such term in the Second Amendment.

"NDA" means a New Drug Application, a Biologics License Application or similar application, as applicable, submitted to the FDA to obtain marketing approval for a pharmaceutical or biologic product in the United States.

"Net Cash Proceeds" means (a) with respect to any Prepayment Event other than in connection with an Equity Sale Milestone, the amount of all Cash proceeds (including deferred compensation) and including securities or other property converted into Cash, in each case received (directly or indirectly) by or on behalf of a Loan Party (if on behalf, then for the account of such Loan Party) or a Platform Company, or distributable to a Loan Party or a Platform Company (to the extent such proceeds which are distributable are not distributed at the direction of such Loan Party or Platform Company or as a result of such Loan Party or Platform Company voting Equity Interests owned in favor of any corporate action that would result in such proceeds not being actually distributed), and (b) with respect to any Prepayment Event in connection with an Equity Sale Milestone, the applicable Equity Sale Premium from such Equity Sale Milestone, in each case, from time to time, as a result of a Prepayment Event occurring after the Closing Date, after deducting therefrom, without duplication, (x) **(1)** reasonable fees, commissions, expenses and other direct costs related thereto and required to be paid or payable by such Loan Party (or the applicable Platform Company or its applicable Subsidiary) in connection with such Prepayment Event (including attorneys' fees, accountants' fees, investment banking fees, survey costs, title insurance premiums, and related search and recording charges, transfer taxes, deed or mortgage recording taxes, other customary expenses and brokerage, consultant and other customary fees actually incurred in connection therewith) **to the extent paid or payable to non-Affiliates and (2) the Budgeted Amount, provided that (A) the Budgeted Amount is deposited into a Controlled Account of a Loan Party no later than** [***] **days after the commencement of the applicable Budgeted Period or, with respect to the Navire Prepayment Event,** [***] **days after the Second Amendment Effective Date; provided that Budgeted Amounts relating to separate Prepayment Events shall each be deposited into an individual Controlled Account and segregated from other such Controlled Accounts, (B) the funds held in such Controlled Account(s) shall be withdrawn and used solely for expenses directly attributable to the performance of obligations by any Platform Company or associated Loan Party(ies) in connection with the applicable Prepayment Event, (C) the Borrower shall comply with Section 7.1(p) and (q), and (D) any Overbudgeted Amount shall be deemed to be "Net Cash Proceeds" subject to prepayment in accordance with Section 2.4(b)(i) at the end of the applicable Budgeted Period or, solely with respect to any Overbudgeted Amount set forth in clause (ii) of the definition thereof, promptly upon the applicable** [***], (y) Taxes paid, payable, or determined by such Loan Party or Platform Company to be payable or attributable for payment in connection with such transaction to any taxing authorities by such Loan Party (or the applicable Platform Company or its applicable Subsidiary), to the extent then paid or payable and reasonably attributable to such transaction, and any repatriation costs associated with receipt or distribution by the applicable taxpayer of such proceeds and (z) any cash reserves required to be maintained by such Loan Party (or the applicable Platform Company or its applicable Subsidiary) in connection with such transaction in accordance with GAAP or applicable law, provided that when any reserve or any portion thereof is no longer required to be maintained such amount shall be considered Net Cash Proceeds then received, and provided further, that such Loan Party (or the applicable Platform Company or its applicable Subsidiary) shall, at Agent's reasonable request, provide such calculations or evidence of costs deducted in arriving at Net Cash Proceeds as Agent may reasonably require to confirm the calculation of Net Cash Proceeds in accordance with the foregoing.

"New Drug Application" means a new drug application filed with the FDA under 21 U.S.C. § 355(b).

"Non-Defaulting Lender" means, at any time, each Lender that is not a Defaulting Lender at such time.

"OFAC" means the U.S. Department of Treasury Office of Foreign Assets Control.

"OFAC Lists" means, collectively, the Specially Designated Nationals and Blocked Persons List maintained by OFAC pursuant to Executive Order No. 13224, 66 Fed. Reg. 49079 (Sept. 25, 2001) and/or any other list of terrorists or other restricted Persons maintained pursuant to any of the rules and regulations of OFAC or pursuant to any other applicable Executive Orders.

"Operating Company" means a Person which is predominantly in the business of research, development, manufacturing, sale or marketing of products and activities substantially related thereto, or a Person holding assets, including without limitation Intellectual Property that are useful for a Person that is predominantly in the line of business described above and in anticipation of such Person commencing operations in such line of business and which Borrower intends to cause to commence operations.

"Organizational Documents" means with respect to any Person, such Person's formation documents, and (a) if such Person is a corporation, its bylaws, (b) if such Person is a limited liability company, its limited liability company agreement (or similar agreement), and (c) if such Person is a partnership, its partnership agreement (or similar agreement), each of the foregoing with all current amendments or modifications thereto.

"Origin" means Origin Biosciences, Inc.

"Other Connection Taxes" means, with respect to any Recipient, Taxes imposed as a result of a present or former connection between such Recipient and the jurisdiction imposing such Tax (other than connections arising from such Recipient having executed, delivered, become a party to, performed its obligations under, received payments under, received or perfected a security interest under, engaged in any other transaction pursuant to or enforced any Loan Document, or sold or assigned an interest in any Loan or Loan Document).

"Other Milestone" means each of the following:

(a) [***]

(b) [***]

(c) [***]

(d) [***]

(e) [***]

in each case of clauses (a) through (e) above, as certified by the Chief Executive Officer or the Chief Financial Officer of Borrower as to the satisfaction of such applicable requirements (and with such certification to be accompanied by reasonably detailed supporting documentation demonstrating that such requirements have been satisfied).

"Other Taxes" means all present or future stamp, court or documentary, intangible, recording, filing or similar Taxes that arise from any payment made under, from the execution, delivery, performance, enforcement or registration of, from the receipt or perfection of a security interest under, or otherwise with respect to, any Loan Document, except any such Taxes that are Other Connection Taxes imposed with respect to an assignment.

"Overbudgeted Amount" means, with respect to any Budgeted Amount for any Prepayment Event, (i) on or prior to the last day of such Budgeted Period, the portion of any such Budgeted Amount that is no longer anticipated or planned to be incurred within such Budgeted Period, as determined by the applicable Loan Party, the Platform Company, or the counterparty to the definitive agreement governing the transaction underlying such Prepayment Event, in each case in its reasonable discretion, (ii) [***] **which gave rise to a Prepayment Event, the portion of any such Budgeted Amount that was not actually incurred during the Budgeted Period and prior to such** [***]**, and (iii) on the day after the last day of such Budgeted Period, the portion of any such Budgeted Amount that was not actually incurred during the Budgeted Period; for the avoidance of doubt, to the extent included in the Budgeted Amount but not actually incurred on or prior to the last day of the Budgeted Period, any prepaid expenses (as determined under GAAP) shall be deemed "Overbudgeted Amount" under this clause (iii). For the purposes of this definition, an amount shall be deemed to be "incurred" only if it is considered a payable in accordance with GAAP and is paid within three (3) months of incurrence.**

"Pass-through Entity" means any holding company of any entity that would constitute a Platform Company, which holding company is wholly-owned by a Loan Party and which holding company does not hold any material assets (other than its direct or indirect Equity Interests in such Platform Company, which Equity Interests in any such Platform Company shall be pledged as Pledged Collateral) or engage in any material operations or business other than as a holding company for one or more Platform Companies.

"Patent License" means any written agreement granting any right with respect to any invention on which a Patent is in existence or a Patent application is pending, in which agreement any Loan Party now holds or hereafter acquires any interest.

"Patents" means all letters patent of, or rights corresponding thereto, in the United States of America or in any other country, all registrations and recordings thereof, and all applications for letters patent of, or rights corresponding thereto, in the United States of America or any other country, and all reisssues, divisions, continuations, renewals, extensions, revisions, reexaminations and continuation-in-parts thereof.

"PATRIOT Act" means the Uniting and Strengthening America by Providing Appropriate Tools Required to Intercept and Obstruct Terrorism Act of 2001, Pub. L. 107-56, signed into law October 26, 2001, as amended from time to time.

"Payment Date" is the first Business Day of each fiscal quarter, commencing on January 3, 2022.

"Perfection Certificate" means that certain perfection certificate dated as of the Closing Date and executed by each of the Loan Parties as of such date (as may be amended, supplemented or otherwise modified from time to time).

"Permitted BB Square Investment" has the meaning set forth in Section 7.6 of this Agreement.

"Permitted Bond Hedge Transaction" means any call or capped call option (or substantively equivalent derivative transaction) relating to Borrower's common stock (or other securities or property following a merger event or other change of the common stock of Borrower) purchased by Borrower in connection with the issuance of any Permitted Convertible Debt and as may be amended in accordance with its terms; provided that, the net purchase price of any such call option transaction less the amount received by Borrower in respect of any Permitted Warrant Transaction in connection with such issuance of Permitted Convertible Debt shall not exceed 20% of the gross proceeds to Borrower from such issuance of Permitted Convertible Debt; provided further that the terms, conditions and covenants of each such call option transaction are customary for agreements of such type; provided further that a certificate of Borrower as to the satisfaction of such requirement (described in the immediately preceding proviso) delivered to Administrative Agent (for delivery to Lenders) at least [***] Business Days prior to entering into such transaction, together with a reasonably detailed description of the material terms, conditions and covenants of such transaction or drafts of documentation relating thereto, stating that Borrower has determined in good faith that such terms, conditions and covenants satisfy the foregoing requirement, shall be conclusive evidence of satisfaction thereof unless Administrative Agent notifies Borrower within such [***] Business Day period that Required Lenders disagree, in their commercially reasonably judgment, with such determination (which notice shall include a description of the basis upon which Required Lenders disagree).

"Permitted Convertible Debt" means Indebtedness of Borrower that is convertible into a fixed number (subject to customary anti-dilution adjustments, "make-whole" increases and other customary changes thereto) of shares of common stock of Borrower (or other securities or property following a merger event or other change of the common stock of Borrower), Cash or any combination thereof (with the amount of such Cash or such combination determined by reference to the market price of such common stock or such other securities); provided that such Indebtedness shall (a) not require any scheduled amortization or otherwise require payment of principal prior to, or have a scheduled maturity date, earlier than, [***] days after the Maturity Date, (b) be unsecured, (c) not be guaranteed by any Subsidiary of Borrower, and (d) be on terms and conditions customary for Indebtedness of such type; provided further that a certificate of Borrower as to the satisfaction of the conditions described in clause (d) delivered to Administrative Agent (for delivery to Lenders) at least [***] Business Days prior to the incurrence of such Indebtedness, together with a reasonably detailed description of the material terms and conditions of such Indebtedness and drafts of documentation relating thereto, stating that Borrower has determined in good faith that such terms and conditions satisfy the foregoing requirements of clause (d), shall be conclusive unless Administrative Agent notifies Borrower within such [***] Business Day period that Required Lenders disagree, in their commercially reasonable judgment, with such determination which notice shall include a description of the basis upon which Required Lenders disagree. For the avoidance of doubt, the Borrower's (i) 2.50% Convertible Senior Notes due 2027 issued pursuant to the indenture dated as of March 9, 2020 between the Borrower and U.S. Bank National Association, as trustee, and (ii) 2.25% Convertible Senior Notes due 2029 issued pursuant to the indenture dated as of January 28, 2021 between the Borrower and U.S. Bank National Association, as trustee, shall both constitute Permitted Convertible Debt.

“Permitted Indebtedness” means:

(a) Indebtedness of any Loan Party in favor of Lenders or Agent arising under this Agreement or any other Loan Document;

(b) Indebtedness existing on the Closing Date which is disclosed in Schedule 1A (other than Indebtedness permitted pursuant to clause (k) below);

(c) Indebtedness to trade creditors incurred in the ordinary course of business;

(d) Subordinated Indebtedness;

(e) reimbursement obligations in connection with letters of credit that are secured by Cash and issued on behalf of a Loan Party or a Subsidiary for real estate purposes in the ordinary course of business in an aggregate amount in respect of such letter of credit reimbursement obligations at any one time outstanding not to exceed $[***];

(f) Indebtedness of the Loan Parties incurred to finance the acquisition of (i) equipment to be used for the development, testing and manufacturing of products, or (ii) other equipment, provided that the aggregate principal amount of Indebtedness outstanding at any time to finance equipment other than as described in subclause (i) shall not exceed $[***];

(g) intercompany Indebtedness among the Loan Parties, provided that (i) that such Indebtedness is subordinated to the Secured Obligations pursuant to the Intercompany Subordination Agreement and (ii) any subsequent transfer or assignment of any such Indebtedness (other than to another Loan Party) or the Loan Party owing such Indebtedness ceasing to be a Loan Party, shall be deemed, in each case, to be an incurrence of such Indebtedness not permitted by this clause (g);

(h) Indebtedness incurred to finance insurance premiums in the ordinary course of business;

(i) Indebtedness incurred as a result of endorsing negotiable instruments received in the ordinary course of business;

(j) [reserved];

(k) Permitted Convertible Debt in an aggregate principal amount not to exceed $[***] at any one time outstanding;

(l) extensions, refinancings and renewals of any Permitted Indebtedness described in clause (b) above, provided that the principal amount of such Indebtedness being extended, refinanced or renewed is not increased or the terms modified to impose materially more burdensome terms upon the applicable Loan Party (including by shortening the maturity or weighted average life to maturity of the Indebtedness being extended, refinanced or renewed), as the case may be;

(m) unsecured Indebtedness of any Loan Party or any of its Subsidiaries in connection with acquisitions permitted pursuant to clause (j) of Permitted Investments (i) consisting of earnouts or similar deferred purchase price (including customary purchase price adjustments and modifications) or (ii) that is issued to a seller of assets or an entity acquired in an acquisition permitted hereunder, provided that (x) such obligations shall be subordinated to the Secured Obligations pursuant to subordination provisions reasonably satisfactory to the Required Lenders and (y) the aggregate amount of all such obligations incurred pursuant to subclauses (i) and (ii) shall not to exceed $[***] at any time outstanding;

(n) unsecured Indebtedness of a Subsidiary owed to a Loan Party or a wholly-owned Subsidiary of a Loan Party, which Indebtedness shall (i) if owed to a Loan Party, be pledged to Agent as Collateral for the Secured Obligations in accordance with the terms hereof and, if requested by the Required Lenders, be evidenced by promissory notes, (ii) be subordinated to the Secured Obligations pursuant to the Intercompany Subordination Agreement and (iii) constitute Permitted Investments and otherwise be permitted hereunder, including under Sections 7.6 and 7.13;

(o) unsecured guarantees of the Loan Parties in respect of Indebtedness of any Loan Party to the extent permitted under Section 7.6;

(p) Indebtedness arising from a bank or other financial institution honoring a check, draft or similar instrument (other than resulting from any overdraft) in the ordinary course of business;

(q) Indebtedness incurred in respect of Cash Management Services, in each case, incurred in the ordinary course of business;

(r) Indebtedness arising under performance, payment, surety, customs, stay, bid or appeal bonds, performance and completion guaranties and similar instruments, in each case in the ordinary course of business and not in connection with any Indebtedness for borrowed money; provided that the aggregate amount of such Indebtedness shall not exceed $[***] at any time outstanding;

(s) Indebtedness consisting of Contingent Obligations in connection with any equity exchange program involving the issuance of equity awards under Borrower’s equity incentive plans;

(t) Permitted Senior Debt;

(u) any (i) royalty financing or similar transaction (including any royalty sale or any synthetic royalty financing) that does not exceed ten (10%) of the net sales in respect of any Product of the applicable Loan Party, or (ii) royalty financing or similar transaction (including any royalty sale or any synthetic royalty financing) by any Platform Company that is not a Loan Party, in each case of the foregoing clauses (i) and (ii), that does not (directly or indirectly, by acceleration or otherwise) result in recourse to any Loan Party or Platform Company prior to the date that is [***] after the Maturity Date, except with respect to the applicable percentage of net sales of the applicable Product that is the subject of such royalty financing or similar transaction, plus any customary fees and expenses payable in connection therewith (each, a “Permitted Royalty Transaction”);

(v) [reserved];

(w) Hedge Agreements (entered into in order to manage existing or anticipated interest rate, foreign exchange rate or commodity price risks and not for speculative purposes), in each case that (i) may be unsecured, (ii) solely in the case of Hedge Agreements in respect of foreign currency exchanges, are secured by Cash in an amount up to $[***] and (iii) are entered into in the ordinary course of business and in conformity with all requirements of applicable laws and regulations and issued on behalf of a Loan Party; and

(x) unsecured Indebtedness of the Loan Parties or, subject to Section 7.4, any of their respective Subsidiaries in an aggregate amount not to exceed $[***], provided that, immediately after giving effect to the incurrence of such Indebtedness, no Default or Event of Default shall have occurred and be continuing.

"Permitted Investment" means:

(a) Investments existing on the Closing Date which are disclosed in Schedule 1B;

(b) (i) marketable direct obligations issued or unconditionally guaranteed by the United States of America or any agency or any State thereof maturing within one year from the date of acquisition thereof currently having a rating of at least A-2 or P-2 from either Standard & Poor's Corporation or Moody's Investors Services, (ii) commercial paper maturing no more than one year from the date of creation thereof and currently having a rating of at least A-2 or P-2 from either Standard & Poor's Corporation or Moody's Investors Services, (iii) certificates of deposit issued by any bank with assets of at least $[***] maturing no more than one year from the date of investment therein, (iv) money market accounts, and (v) Investments permitted by any Loan Party's investment policy, provided that the Required Lenders have approved such investment policy in writing (such approval not to be unreasonably withheld, conditioned or delayed) (collectively, "Cash Equivalents");

(c) repurchases by a Loan Party of its Equity Interests or the Equity Interests of any of its Subsidiaries in an aggregate amount not to exceed the Available Investment Amount in any Available Investment Period, in each case subject to the satisfaction of the Equity Cash Payment Conditions;

(d) Investments accepted by a Loan Party in connection with Permitted Transfers;

(e) Investments received in connection with the bankruptcy or reorganization of a customer or supplier in the ordinary course of business;

(f) Investments consisting of notes receivable of the Loan Parties, or prepaid royalties and other credit extensions made by the Loan Parties in the ordinary course of business, in an aggregate amount not to exceed $[***] at any one time outstanding;

(g) loans and advances to, or guarantees of Indebtedness of, employees, directors, officers, managers, consultants or independent contractors in the ordinary course of business in an amount not to exceed $[***] at any one time outstanding;

(h) Investments by any Loan Party in another Loan Party;

(i) Investments in Deposit Accounts, subject to compliance with Section 7.12 hereof;

(j) subject to compliance with Section 7.13, Investments in previously formed or acquired Platform Companies that are not Loan Parties (including such Platform Companies existing on the Closing Date, and whether as a result of a formation of a Platform Company, the purchase of additional Equity Interests of a Platform Company, the formation of or contribution to a joint venture or any other capital contribution to a Platform Company), including (for the avoidance of doubt), loans to or other Investments in such Platform Companies for operating purposes in the ordinary course of business; provided that any such Investments in joint ventures shall be subject to the requirements specified in clause (ii) to the proviso to clause (y) of this definition below;

(k) Borrower's entry into (including payments of premiums in connection therewith), and the performance of obligations under, any Permitted Bond Hedge Transactions and Permitted Warrant Transactions in accordance with their terms;

(l) to the extent constituting an Investment, Investments consisting of Indebtedness, Liens, Dispositions or distributions permitted under Section 7.4, Section 7.5, Section 7.6 or Section 7.7;

(m) Investments consisting of purchases or acquisitions of inventory, supplies, materials and equipment, in each case in the ordinary course of business;

(n) extensions of trade credit in the ordinary course of business by any Loan Party;

(o) Investments in connection with the cash management operations of any Loan Party and its Subsidiaries that constitute Permitted Indebtedness;

(p) Licenses described in clause (b) of the defined term "Permitted Transfer";

(q) guarantees of operating leases or of other obligations of any Loan Party permitted under this Agreement that do not constitute Indebtedness, in each case, entered into by any Loan Party in the ordinary course of business;

(r) subject to compliance with Section 7.13, Investments made solely with Equity Interests of Borrower as consideration for the purchase or other acquisition of Equity Interests or debt or other securities of another Person (including in connection with any Acquisitions) which such other Person would be, immediately after giving effect to such Investment, an Operating Company that is majority-owned by one or more Loan Parties; provided that any such Investments in joint ventures shall be subject to the requirements specified in clause (ii) to the proviso to clause (y) of this definition below;

(s) [reserved];

(t) Investments constituting the cashless repurchase of common stock of Borrower deemed to occur upon the exercise of options, warrants or similar rights solely to the extent that shares of such stock represent a portion of the exercise price of such options, warrants or similar rights;

(u) Investments consisting of the exchange of Equity Interests of Borrower for the Equity Interests of an Affiliate;

(v) Investments consisting of Contingent Obligations to the extent constituting Permitted Indebtedness;

(w) additional Investments that do not exceed $[***] in the aggregate per fiscal year, provided that, immediately after giving effect to the making of such Investment, no Default or Event of Default shall have occurred and be continuing;

(x) subject to compliance with Section 7.13, Investments in Pass-through Entities; and

(y) any other Investment (including the acquisition of new Platform Companies, Investments in joint ventures that are Operating Companies, the acquisition of the Equity Interests of any Person that is an Operating Company, loans to a Platform Company, or the acquisition of, or the right to use, develop, or License any Intellectual Property), other than repurchases by a Loan Party of its Equity Interests or the Equity Interests of any of its Subsidiaries, Investments in joint ventures or other Persons that are not (immediately after giving effect to such Investment) Operating Companies which are majority-owned by one or more Loan Parties or the acquisition of (or other Investment in) the Equity Interests of any Person that is not (immediately after giving effect to such Investment) an Operating Company which is majority-owned by one or more Loan Parties, in an aggregate amount not to exceed the Available Investment Amount in any Available Investment Period; provided that (i) immediately after giving effect to such Investment, no Event of Default shall have occurred and be continuing and the Loan Parties' Qualified Cash shall be equal to or greater than $[***] and (ii) to the extent such Investments are in joint ventures or other Persons that are Operating Companies or for the acquisition of Equity Interests of any Person that is an Operating Company (including the acquisition of new majority-owned Platform Companies), (A) all Equity Interests and other ownership interests held by a Loan Party in any such joint venture or other Person shall constitute Pledged Collateral, (B) all representations and warranties set forth in Section 5.15 shall be true and correct with respect to such Pledged Collateral, (C) solely with respect to such Investments in joint ventures in excess of $[***] per joint venture or $[***] in the aggregate for all joint ventures (in each case, excluding any Investments in joint ventures satisfying the following clauses (x) and (y)), (x) the Loan Parties have taken all steps necessary to permit Agent to become a "transferee" under the relevant joint venture or other Organizational Documents if Agent exercises its remedies with respect to such joint venture or other Equity Interest and (y) no further consent, approval, authorization or other order of any Person and no consent or authorization of any governmental authority or regulatory body shall be required to be made or obtained by any Loan Party either (I) for the pledge by such Loan Party of such Pledged Collateral pursuant to this Agreement or (II) for the exercise by Agent or Lenders of the voting or other rights provided for this Agreement or the remedies in respect of the Pledged Collateral pursuant to this Agreement, except for those which have been obtained and (D) the pledge, grant of a security interest in, and delivery of such Pledged Collateral to Agent pursuant to this Agreement will create a valid first priority Lien on and in such Pledged Collateral;

provided further that no Loan Party shall make Investments in any Platform Company that is not a Loan Party that is in default with respect to Indebtedness in excess of $[***] except for (x) Equity Cure Investments of up to $[***] for any such Platform Company and up to $[***] in the aggregate for all Platform Companies that are not Loan Parties (which such Equity Cure Investments, if made, shall be made as an Investment in reliance on clause (y) of this definition), (y) to fund any mandatory legal and regulatory expenses of a Platform Company that is not a Loan Party when due, or (z) as otherwise approved by the Required Lenders in writing.

Notwithstanding anything herein to the contrary, to the extent any Platform Company, other Subsidiary of the Borrower or any joint venture is required to become a Guarantor pursuant to Section 7.13, then no further Investments may be made in such Platform Company, other Subsidiary of the Borrower or any joint venture until such Platform Company, other Subsidiary of the Borrower or any joint venture has become a Guarantor in accordance with this Agreement.

"Permitted Liens" means any and all of the following:

(a) Liens in favor of Agent or Lenders;

(b) Liens existing on the Closing Date which are disclosed in Schedule 1C;

(c) Liens arising by operation of law in favor of materialmen, artisans, mechanics, carriers warehouseman, landlords and other Persons securing ordinary course obligations which are not yet delinquent and not in connection with borrowed money;

(d) Liens for Taxes, fees, assessments or other governmental charges or levies, either (i) not delinquent or (ii) being contested in good faith by appropriate proceedings, provided that the Loan Parties maintain adequate reserves therefor in accordance with GAAP;

(e) Liens arising from judgments, decrees or attachments (or appeal or other surety bonds related to such judgments) in circumstances which do not constitute an Event of Default hereunder;

(f) the following deposits, to the extent made in the ordinary course of business: deposits under worker's compensation, unemployment insurance, social security and other similar laws, or to secure the performance of bids, tenders or contracts (other than for the repayment of borrowed money) or to secure indemnity, performance or other similar bonds for the performance of bids, tenders or contracts (other than for the repayment of borrowed money) or to secure statutory obligations (other than Liens arising under ERISA or environmental Liens) or surety or appeal bonds, or to secure indemnity, performance or other similar bonds;

(g) leasehold interests in leases or subleases and licenses granted in the ordinary course of business and not interfering in any material respect with the business of the licensor;

(h) Liens on equipment, software embedded in such equipment, and proceeds thereof, which (i) secure Permitted Indebtedness described in clause (f) of the defined term "Permitted Indebtedness" above, or (ii) exist at the time such equipment is acquired by a Loan Party;

(i) Liens in favor of customs and revenue authorities arising as a matter of law to secure payment of custom duties that are promptly paid on or before the date they become due;

(j) Liens in connection with Indebtedness described in clause (h) of the defined term "Permitted Indebtedness," provided that such Lien is limited to insurance proceeds arising from the subject insurance policy and the unearned portion of premium payments;

(k) statutory and common law rights of set-off and other similar rights as to deposits of Cash and securities in favor of banks, other depository institutions and brokerage firms or securities intermediaries solely to secure payment of amounts due in the ordinary course of business in connection with the maintenance of Deposit Accounts or securities accounts;

(l) easements, servitudes, zoning restrictions, rights-of-way and similar encumbrances on real property imposed by law or arising in the ordinary course of business so long as they do not materially impair the value or marketability of the related property;

(m) Licenses permitted hereunder;

(n) (i) Liens on Cash securing obligations permitted in accordance with clause (e) of the defined term “Permitted Indebtedness” in an aggregate amount not to exceed the reimbursement obligations secured thereby, and (ii) security deposits in connection with real property incurred in the ordinary course of business;

(o) Liens incurred in connection with the extension, renewal or refinancing of the Indebtedness secured by Liens of the type described in clause (b) above; provided, that any extension, renewal or replacement Lien shall be limited to the property encumbered by the existing Lien and the principal amount of the Indebtedness being extended, renewed or refinanced (as may have been reduced by any payment thereon) does not increase, and subject to any limitation with respect to the amount secured by such Lien of such type, to the extent described in one of the foregoing clauses of this defined term;

(p) Liens of Permitted Senior Debt Holders encumbering solely the Permitted Senior Debt Priority Collateral securing Permitted Senior Debt;

(q) Liens in connection with Indebtedness described in clause (w) of the defined term “Permitted Indebtedness” consisting of Cash securing such Indebtedness issued on behalf of a Loan Party;

(r) [reserved];

(s) (i) with respect to any [***] that is structured as a “true sale”, precautionary Liens on the applicable percentage of net sales of the applicable Product or (ii) with respect to any [***] that is not structured as a “true sale”, Liens on (x) the applicable percentage of net sales of the applicable Product that is the subject of such [***] or (y) any other asset of the applicable Loan Party or Platform Company party to such [***] relating to the applicable Product that is the subject of such [***] so long as such Liens are subordinated to the Liens securing the Secured Obligations pursuant to an intercreditor agreement with Agent on terms and conditions reasonably acceptable to the Required Lenders; and

(t) to the extent constituting Liens, restrictions arising under applicable securities laws as a result of any Loan Party’s any/or any Agent’s or Lender’s status as an “affiliate” and/or “insider” of the issuer of any Equity Interests constituting Collateral and/or the status of any Equity Interests constituting Collateral as “restricted securities” under Rule 144 promulgated under the United States Securities Act of 1933, as amended.

“Permitted Royalty Transaction” has the meaning set forth in clause (u) of the definition of “Permitted Indebtedness.”

“Permitted Senior Debt” means senior secured Indebtedness of the Loan Parties in the form of an asset-based revolving credit facility in a maximum principal amount not to exceed $[***] at any one time outstanding incurred under the Permitted Senior Debt Documents which satisfies the following requirements: (a) Borrower shall have delivered to Agent and the Lenders all material Permitted Senior Debt Documents concurrently with its entry into such Permitted Senior Debt Documents, certified by an officer of Borrower, and (b) such Indebtedness shall be secured solely by the Loan Parties’ accounts receivable, inventory and ancillary rights required for the exercise of remedies with respect to the foregoing of the Loan Parties and proceeds thereof (the “Permitted Senior Debt Priority Collateral”).

"Permitted Senior Debt Priority Collateral" has the meaning set forth in the definition of "Permitted Senior Debt."

"Permitted Senior Debt Documents" means each agreement, instrument and document entered into by any Loan Party in connection with the Permitted Senior Debt, as the same may be amended, modified, extended, restated, replaced or supplemented from time to time, and which agreements, instruments and documents shall include (and, as applicable, be subject to) the terms and provisions of an intercreditor agreement in form and substance reasonably acceptable to the Required Lenders in their reasonable discretion in connection therewith.

"Permitted Senior Debt Holder" means any holder of Permitted Senior Debt or any agent thereof.

"Permitted Transfers" means:

(a) Dispositions of Inventory in the ordinary course of business;

(b) subject to the terms of Section 7.8, exclusive or non-exclusive Licenses and similar arrangements for the use of Intellectual Property in the ordinary course of business (including in connection with business development transactions;

(c) Dispositions of worn-out, obsolete or surplus Equipment at fair market value in the ordinary course of business;

(d) use of Cash in the ordinary course of business in a manner not prohibited by the terms of this Agreement;

(e) Dispositions by any Loan Party of Investments in Platform Companies in accordance with such Loan Party's Organizational Documents;

(f) Dispositions (i) among the Loan Parties, (ii) by a Subsidiary that is not a Loan Party to a Loan Party, (iii) subject to the terms of Section 7.8, consisting of Permitted Investments in a Platform Company by a Loan Party, or (iv) subject to the terms of Section 7.8, consisting of assets other than Investments or Material Intellectual Property by and to a Platform Company to and from a Loan Party in the ordinary course of business;

(g) Dispositions of the Equity Interests of [***]or all or substantially all of the assets of [***];

(h) Dispositions of any or all of Borrower's rights and title to the [***];

(i) other Dispositions of assets having a fair market value of not more than $[***] in the aggregate in any fiscal year, provided that, immediately after giving effect to such Disposition, no Default or Event of Default shall have occurred and be continuing;

(j) Permitted Royalty Transactions; and

(k) Dispositions of the Existing Priority Review Voucher or any other Priority Review Voucher.

“Permitted Warrant Transaction” means any call option, warrant or right to purchase (or substantively equivalent derivative transaction) relating to Borrower’s common stock (or other securities or property following a merger event or other change of the common stock of Borrower) and/or Cash (in an amount determined by reference to the price of such common stock) sold by Borrower substantially concurrently with any purchase by Borrower of a related Permitted Bond Hedge Transaction and as may be amended in accordance with its terms; provided that (x) the terms, conditions and covenants of each such call option transaction are customary for agreements of such type, as determined by Lender in its commercially reasonable discretion and (y) such call option transaction would be classified as an equity instrument in accordance with GAAP; provided further that a certificate of Borrower as to the satisfaction of such requirement (described in the immediately preceding proviso) delivered to Administrative Agent (for delivery to Lenders) at least [***] Business Days prior to the entry into such transaction, together with a reasonably detailed description of the material terms, conditions and covenant of such transaction or drafts of documentation relating thereto, stating that Borrower has determined in good faith that such terms, conditions and covenants satisfy the foregoing requirement, shall be conclusive unless Agent notifies Borrower within such [***] Business Day period that Agent notifies Borrower within such [***] Business Day period that Required Lenders disagree, in their commercially reasonable judgment, with such determination which notice shall include a description of the basis upon which Required Lenders disagree).

“Person” means any individual, sole proprietorship, partnership, joint venture, trust, unincorporated organization, association, corporation, limited liability company, institution, other entity or government.

“Phase 1 Clinical Trial” means a clinical trial that generally provides for the first introduction into humans of a pharmaceutical or biologic product with the primary purpose of determining safety, metabolism and pharmacokinetic properties and clinical pharmacology of such product, in a manner that is generally consistent with 21 CFR § 312.21(a), as amended (or its successor regulation).

[***]

“Phase 3 Study” means with respect to a clinical trial evaluating a drug, any clinical trial initiated after preliminary evidence suggesting effectiveness of such drug has been obtained, conducted to gather the additional information about effectiveness and safety that is needed to evaluate the overall benefit-risk relationship of such drug and to provide an adequate basis for physician labeling.

“PIK Interest” means interest payable in-kind by adding an amount equal to the applicable percentage of the Applicable Rate of the outstanding principal balance of the Term Loan Advances to the then outstanding principal balance of the applicable Term Loan Advances on a quarterly basis on each applicable Payment Date so as to increase the outstanding principal balance of such Term Loan Advances (which such capitalized principal in the form of PIK Interest shall accrue interest from and including the Payment Date on which such PIK Interest is added to the Term Loan Advance at the Applicable Rate).

“Pivotal Clinical Trial” means a clinical trial with a defined dose or a set of defined doses of a pharmaceutical or biologic product designed to ascertain efficacy and safety of such product, in a manner that is generally consistent with 21CFR § 312.21(c), as amended (or its successor regulation), for the purpose of enabling the preparation and submission of an NDA.

“Platform Company” means any Operating Company in the life sciences or healthcare sector and focused on the development and commercialization of products, and in which a Loan Party has made an Investment (whether by capital contribution, the acquisition of the Equity Interests thereof, a Disposition of assets thereto, or in connection with a joint venture, corporate collaboration or similar corporate structure) in accordance with the terms of this Agreement, its Organizational Documents and consistent in all material respects with past practices, including each Operating Company in which Loan Party maintains an Investment as of the Closing Date.

"Pledged Collateral" means:

(a) all Equity Interests now owned or hereafter acquired by a Loan Party to the extent not constituting Excluded Collateral;

(b) with respect to any limited liability company membership units or general or limited partnership interests now owned or hereafter acquired by a Loan Party: (i) all payments or distributions whether in Cash, property or otherwise, at any time owing or payable to such Loan Party on account of its interest as a member or partner, as the case may be, in any of the issuers of such Equity Interests or in the nature of a management or other fee paid or payable by any of such issuers to such Loan Party; (ii) all of such Loan Party's rights and interests under each of the Organizational Documents, including all voting and management rights and all rights to grant or withhold consents or approvals; (iii) all rights of access and inspection to and use of all books and records, including computer software and computer software programs, of each of such issuers;

(iv) all other rights, interests, property or claims to which such Loan Party may be entitled in its capacity as a partner or a member of any such issuer; and (v) all proceeds, income from, increases in and products of any of the foregoing, in each case subject to the terms of this Agreement;

(c) all additional Equity Interests from time to time acquired or formed by a Loan Party in any manner (which additional Equity Interests shall be deemed to be part of the Pledged Collateral whether or not Schedule 5.15 has been updated in accordance with this Agreement) to the extent constituting Collateral, and any certificates, if applicable, representing such additional Equity Interests;

(d) all rights and interests of a Loan Party in respect of a joint venture; and

(e) all dividends, distributions, cash, instruments and other property or proceeds from time to time received, receivable or otherwise distributed in respect of or in exchange for any or all of such Equity Interests, in each case subject to the terms of this Agreement.

"Prepayment Charge" has the meaning assigned to such term in Section 2.4(a).

"Prepayment Event" means, with respect to any transaction consummated after the Closing Date, (i) any Disposition of Pledged Collateral ~~to the extent the Net Cash Proceeds for all such transactions, whether in a single transaction or series of related transactions, exceed (x) prior to the~~ [***] ~~Milestone Date, $~~[***] ~~in any fiscal year and (y) from and after the~~ [***] ~~Milestone Date, $~~[***] ~~in any fiscal year,~~, (ii) any Disposition of Collateral (other than Pledged Collateral, assets covered in clause (iii) below or Intellectual Property specified in clause (iv) below) ~~to the extent the Net Cash Proceeds for all such transactions, whether in a single transaction or series of related transactions, exceed (x) prior to the~~ [***] ~~Milestone Date, $~~[***] ~~in any fiscal year and (y) from and after the~~ [***] ~~Milestone Date, $~~[***] ~~in any fiscal year~~, (iii) any Disposition by a Platform Company, any Loan Party or any of their Subsidiaries of assets (including Intellectual Property, but without duplication of clause (iv) below) of such Platform Company, Loan Party or Subsidiary, to the extent ~~(x)~~ the subject assets constitute all or a material part of the applicable entity's assets, on a consolidated basis ~~and (y) Net Cash Proceeds for all such transactions, whether in a single transaction or in a series of related transactions, *plus* any Equity Sale Premium (without duplication of any Equity Sale Premium applied in clause (iv) of this definition below) exceed $~~[***] ~~in any fiscal year in the aggregate~~, (iv) any Disposition of Intellectual Property by any Person that is a Loan Party on the Closing Date, ~~to the extent the Net Cash Proceeds for all such transactions, whether in a single transaction or in a series of related transactions, *plus* any Equity Sale Premium (without duplication of any Equity Sale Premium applied in clause (iii) of this definition above), exceed (x) prior to the~~ [***] ~~Milestone Date, $~~[***] ~~in any fiscal year and (y) from and after the~~ [***] ~~Milestone Date, $~~[***] ~~in any fiscal year,~~ (v) the repurchase or redemption of Pledged Collateral by a Pass-through Entity, Platform Company or Loan Party, (vi) any Permitted Royalty Transaction, except to the extent such transaction relates to Acoramidis or (vii) the receipt of any Equity Sale Premium in connection with the issuance or sale of Equity Interest of the Borrower in connection with any Equity Sale Milestone~~, provided that the Net Cash Proceeds for any such issuance or sale (other than in connection with any Disposition of the Existing Priority Review Voucher) shall be deemed to be the receipt of Net Cash Proceeds pursuant to clause (iii) or (iv), as applicable, of this definition above (and be subject to the same applicable thresholds specified in such clause (iii) or (iv))~~; provided that, notwithstanding anything to the contrary herein, (A) any non-exclusive Licenses granted in the ordinary course of business and not for purposes of commercializing any Intellectual Property (including for purposes of joint development, manufacturing, distribution, partnership or similar purposes, including any licensing transactions with contract research organizations or contract manufacturing organizations), (B) any Licenses, sublicenses and similar and customary arrangements for the use of Intellectual Property solely in connection with contract manufacturing, contract research, distribution, supplier and other similar arrangements that are entered into in the ordinary course of business and not in connection with any monetization or revenue-specific purpose and for which no Loan Party, Platform Company or Pass-through Entity will receive any consideration (whether in the form of cash, equity or otherwise), shall not constitute a Prepayment Event and (C) any Disposition of the Existing Priority Review Voucher shall not constitute a Prepayment Event.

"Priority Review Voucher" means a voucher issued by the FDA to the sponsor of a rare pediatric disease product application, as such term is defined in 21 U.S.C. § 360ff, which entitles the holder of such voucher to priority review of a New Drug Application or Biologics License Application after the date of approval of the rare pediatric disease product application.

"Products" means all products, software, service offerings, technical data or technology currently being designed, manufactured or sold by a Platform Company or any of its Subsidiaries or which a Platform Company or such Subsidiary intends to Dispose of, or distribute, in the future including any products or service offerings under development, collectively, together with all products, software, service offerings, technical data or technology that have been sold, licensed or distributed by a Platform Company since each of its formation.

"Publicity Materials" has the meaning set forth in Section 11.18.

"QED" means QED Therapeutics, Inc.

"QFC" has the meaning assigned to the term "qualified financial contract" in, and shall be interpreted in accordance with, 12 U.S.C. § 5390(c)(8)(D).

"Qualified Cash" means the amount of the Loan Parties' unrestricted Cash held in accounts subject to an Account Control Agreement.

"RDEB" means recessive dystrophic epidermolysis bullosa.

"Receivables" means (i) all of each Loan Party's Accounts, Instruments, Documents, Chattel Paper, Supporting Obligations, letters of credit, proceeds of any letter of credit, and Letter of Credit Rights, and (ii) all customer lists, software, and business records related thereto.

"Recipient" means Agent, any Lender or any other recipient of any payment to be made by or on account of the Secured Obligations.

"Refinancing" means the prepayment in full of all amounts borrowed under the Hercules Loan Agreement, the termination of all commitments thereunder and the release of all security interests and guaranties in connection therewith.

"Register" has the meaning given to it in Section 11.7.

"Required Lenders" means at any time, the holders of more than 50.1% of the aggregate total amount of the outstanding principal amount of the Term Loan Advances of all Lenders then outstanding and the unused Term Commitments of all Lenders; *provided*, in any event, Required Lenders shall include at least two Lenders who are not Affiliates of each other.

"Required Prepayment Date" has the meaning given to it in Section 2.4(c).

"Resolution Authority" means an EEA Resolution Authority or, with respect to any UK Financial Institution, a UK Resolution Authority.

"Sanctioned Country" means, at any time, a country or territory which is the subject or target of any Sanctions.

"Sanctioned Person" means, at any time, (a) any Person listed in any Sanctions-related list of designated Persons maintained by the Office of Foreign Assets Control of the U.S. Department of the Treasury or the U.S. Department of State, or by the United Nations Security Council, the European Union or any EU member state, (b) any Person operating, organized or resident in a Sanctioned Country or (c) any Person controlled by any such Person.

"Sanctions" means economic or financial sanctions or trade embargoes imposed, administered or enforced from time to time by (a) the U.S. government, including those administered by the Office of Foreign Assets Control of the U.S. Department of the Treasury or the U.S. Department of State, or (b) the United Nations Security Council, the European Union or Her Majesty's Treasury of the United Kingdom.

"Second Amendment" means the Second Amendment to Loan and Security Agreement, dated as of the Second Amendment Effective Date, among Borrower, the Guarantors, the Lenders, the Administrative Agent and the Collateral Agent.

"Second Amendment Effective Date" means November 30, 2022.

"Secured Obligations" means the unpaid principal of and interest on (including interest accruing after the maturity of the Loans and interest accruing after the filing of any petition in bankruptcy, or the commencement of any insolvency, reorganization or like proceeding, relating to any Loan Party, whether or not a claim for post-filing or post-petition interest is allowed or allowable in such proceeding) the Loans and all other obligations and liabilities of the Loan Parties to the Agent, and any other Lender, whether direct or indirect, absolute or contingent, due or to become due, or now existing or hereafter incurred, which may arise under, out of, or in connection with, this Agreement or any other Loan

Document, whether on account of principal, interest, any premium (including, without limitation, any Prepayment Charge), reimbursement obligations, payment obligations, fees, indemnities, costs and expenses (including all reasonable and documented out-of-pocket fees, charges and disbursements of counsel to the Agent or any other Lender), but excluding any warrant or other equity investment.

"Secured Parties" means, collectively, the Agents and the Lenders.

"Services Company" has the meaning given to such term in the preamble to this Agreement.

"Signature Law" has the meaning given to such term in Section 11.15.

"Subordinated Indebtedness" means Indebtedness subordinated to the Secured Obligations in amounts and on terms and conditions (including as to maturity) satisfactory to the Required Lenders in their reasonable discretion and subject to a subordination agreement in form and substance reasonably satisfactory to the Required Lenders in their discretion on customary deep subordination terms.

"Subsidiary" means an entity, whether corporate, partnership, limited liability company, joint venture or otherwise, in which a Loan Party owns or controls, directly or indirectly, 50% or more of the outstanding voting securities.

"Taxes" means all present or future taxes, levies, imposts, duties, deductions, withholdings (including backup withholding), assessments, fees or other charges imposed by any governmental authority, including any interest, additions to tax or penalties applicable thereto.

"Term Commitment" means as to any Lender, the obligation of such Lender, if any, to make a Term Loan Advance to Loan Parties as set forth in Section 2.1.

"Term Loan Advance" or "Term Loan Advances" means, individually or collectively, as the context may require, the Tranche I Advance and/or any Tranche II Advance.

"Term Note" means a Secured Term Promissory Note in substantially the form of Exhibit B.

"Trademark License" means any written agreement granting any right to use any Trademark or Trademark registration, now owned or hereafter acquired by a Loan Party or in which a Loan Party now holds or hereafter acquires any interest.

"Trademarks" means all trademarks (including service marks and trade dress), other source or business identifier, whether registered, common law or otherwise, and any applications of the same now or hereafter existing, created, acquired or held in connection therewith, including registrations, recordings and applications in the United States Patent and Trademark Office or in any similar office or agency of the United States of America, any State thereof or any other country or any political subdivision thereof.

"Tranche I Advance" has the meaning set forth in Section 2.1(a)(i).

"Tranche I Term Commitment" means as to any Lender, the obligation of such Lender, if any, to make a Term Loan Advance to the Loan Parties in a principal amount not to exceed the amount set forth under the heading "Tranche I Term Commitment" opposite such Lender's name on Schedule 1.1.

"Tranche II Advance" has the meaning set forth in Section 2.1(a)(ii).

"Tranche II Term Commitment" means as to any Lender, the obligation of such Lender, if any, to make a Term Loan Advance to the Loan Parties in a principal amount not to exceed the amount set forth under the heading "Tranche II Term Commitment" opposite such Lender's name on Schedule 1.1.

"Treasury Rate" means with respect to the Make-Whole Amount, as of the date of the prepayment notice with respect to such prepayment, a rate equal to the then-current yield to maturity (as compiled and published in the most recent Federal Reserve Statistical Release H.15 (519) (or is obtainable from the Federal Reserve System's Data Download Program as of the date of such H.15 (519)) that has become publicly available at least [***] Business Days prior to such date (or, if such Federal Reserve Statistical Release is no longer published, any publicly available source of similar market data)) of actively traded U.S. Treasury securities having a constant maturity and having a duration equal to (or the nearest available tenor) the period from the date that payment is received to the date that falls on the first anniversary of the Closing Date; provided, however, that if the period from the date that payment is received to the date that falls on the first anniversary of the Closing Date is less than one year, then the weekly average yield on actually traded U.S. Treasury securities adjusted to a constant maturity of one year shall be used; provided, further, that in no case shall the Treasury Rate be less than zero.

"UCC" means the Uniform Commercial Code as the same is, from time to time, in effect in the State of New York; provided, that in the event that, by reason of mandatory provisions of law, any or all of the attachment, perfection or priority of, or remedies with respect to, Collateral Agent's Lien on any Collateral is governed by the Uniform Commercial Code as the same is, from time to time, in effect in a jurisdiction other than the State of New York, then the term "UCC" shall mean the Uniform Commercial Code as in effect, from time to time, in such other jurisdiction solely for purposes of the provisions thereof relating to such attachment, perfection, priority or remedies and for purposes of definitions related to such provisions.

"UK Financial Institution" means any BRRD Undertaking (as such term is defined under the PRA Rulebook (as amended from time to time) promulgated by the United Kingdom Prudential Regulation Authority) or any person falling within IFPRU 11.6 of the FCA Handbook (as amended from time to time) promulgated by the United Kingdom Financial Conduct Authority, which includes certain credit institutions and investment firms, and certain affiliates of such credit institutions or investment firms.

"UK Resolution Authority" means the Bank of England or any other public administrative authority having responsibility for the resolution of any UK Financial Institution.

"United States" and "U.S." mean the United States of America.

"U.S. Person" means any Person that is a "United States person" as defined in Section 7701(a)(30) of the Code.

"U.S. Tax Compliance Certificate" has the meaning specified in Section 2.8(d).

"Waivable Mandatory Prepayment" has the meaning given to it in Section 2.4(c).

"Withholding Agent" means Borrower or Agent.

"Write-Down and Conversion Powers" means, (a) with respect to any EEA Resolution Authority, the write-down and conversion powers of such EEA Resolution Authority from time to time under the Bail-In Legislation for the applicable EEA Member Country, which write-down and conversion powers are described in the EU Bail-In Legislation Schedule, and (b) with respect to the United Kingdom, any powers of the applicable Resolution Authority under the Bail-In Legislation to cancel, reduce, modify or change the form of a liability of any UK Financial Institution or any contract or instrument under which that liability arises, to convert all or part of that liability into shares, securities or obligations of that person or any other person, to provide that any such contract or instrument is to have effect as if a right had been exercised under it or to suspend any obligation in respect of that liability or any of the powers under that Bail-In Legislation that are related to or ancillary to any of those powers.

Unless otherwise specified, all references in this Agreement or any Annex or Schedule hereto to a "Section," "subsection," "Exhibit," "Annex," or "Schedule" shall refer to the corresponding Section, subsection, Exhibit, Annex, or Schedule in or to this Agreement. Unless otherwise specifically provided herein, any accounting term used in this Agreement or the other Loan Documents shall have the meaning customarily given such term in accordance with GAAP, and all financial computations hereunder shall be computed in accordance with GAAP, consistently applied. Unless otherwise defined herein or in the other Loan Documents, terms that are used herein or in the other Loan Documents and defined in the UCC shall have the meanings given to them in the UCC. For all purposes under the Loan Documents, in connection with any division or plan of division under Delaware law (or any comparable event under a different jurisdiction's laws): (a) if any asset, right, obligation or liability of any Person becomes the asset, right, obligation or liability of a different Person, then it shall be deemed to have been Disposed of from the original Person to the subsequent Person and (b) if any new Person comes into existence, such new Person shall be deemed to have been organized on the first date of its existence by the holders of its Equity Interests at such time.

Notwithstanding anything to the contrary in this Agreement or any other Loan Document, all terms of an accounting or financial nature used herein shall be construed, and all computations of amounts and ratios referred to herein shall be made without giving effect to any treatment of Indebtedness in respect of convertible debt instruments under Accounting Standards Codification 470-20 (or any other Accounting Standards Codification or Financial Accounting Standard having a similar result or effect) to value any such Indebtedness in a reduced or bifurcated manner as described therein, and such Indebtedness shall at all times be valued at the full stated principal amount thereof. For the avoidance of doubt, and without limitation of the foregoing, Permitted Convertible Debt shall at all times be valued at the full stated principal amount thereof and shall not include any reduction or appreciation in value of the shares deliverable upon conversion thereof.

SECTION 2. THE LOAN

2.1 Term Loan Advance.

(a) Term Commitments.

(i) *Tranche I Term Loan Advance*. Subject to the terms and conditions of this Agreement, the Lenders will severally (and not jointly) make in an amount not to exceed their respective Tranche I Term Commitments, and Borrower agrees to draw, a Term Loan Advance in an aggregate principal amount of $450,000,000 on the Closing Date (the "Tranche I Advance").

(ii) *Tranche II Term Loan Advance*. Subject to the terms and conditions of this Agreement, upon the [***], Borrower may at any time on or prior to December 31, 2022 (the "Delayed Draw Expiration Date") request and the Lenders shall severally (and not jointly) make, in amounts not to exceed their respective unused Tranche II Term Commitments, additional Term Loan Advances (each such advance, a "Tranche II Advance"); provided that (A) prior to [***], the aggregate principal amount of Tranche II Advances shall not exceed $25,000,000, (B) prior to [***], the aggregate principal amount of Tranche II Advances shall not exceed $50,000,000, (C) prior to [***], the aggregate principal amount of Tranche II Advances shall not exceed $75,000,000 and (D) Borrower shall not be entitled to request more than four (4) Tranche II Advances.

(iii) For the avoidance of doubt, upon the making of any Tranche II Advance, the Tranche I Advance and any Tranche II Advance(s) will (other than expressly specified herein, including as specified in Section 2.4(b) hereof) be considered one single class of fungible Loan with identical terms hereunder and under the other Loan Documents.

(b) Advance Request. Borrower shall complete, sign and deliver to Administrative Agent an Advance Request not later than 1:00 p.m., New York time, at least [***] Business Days before the Advance Date of each Term Loan Advance (provided that the Tranche I Term Loan Advance to be made on the Closing Date may be made on such shorter notice as may be agreed by Agent and the Lenders holding a Tranche I Term Commitment and any Tranche II Advance to be made after the Closing Date (but on or prior to the Delayed Draw Expiration Date) may be made on such shorter notice as may be agreed by Agent and all Lenders holding a Tranche II Term Commitment on the date of such Advance Request). Each Lender (or, if agreed among the applicable Lenders, a fronting bank for the Lenders) shall fund the Term Loan Advance up to its respective unused and applicable Term Commitment in the manner requested by the Advance Request provided that each of the conditions precedent to such Term Loan Advance is satisfied or waived as of the respective Advance Date.

(c) Interest. Subject to Section 2.3, the principal amount outstanding under the Term Loan Advances shall accrue interest at a fixed per annum rate equal to the Applicable Rate, which interest shall be payable in cash (other than PIK Interest, which will be capitalized by capitalizing such interest and adding such capitalized interest to the then outstanding principal amount of the applicable Term Loan Advances which shall, from and after the date when added to such principal amount, bear interest in accordance with this Section 2.1(c)) quarterly in arrears in accordance with Sections 2.1(d) and 2.3, based on a year consisting of three hundred sixty (360) days, with interest computed daily based on the actual number of days elapsed. In order to elect to pay PIK Interest, Borrower must deliver to Lenders at least [***] Business Days prior to the applicable Payment Date, a certificate that is executed by an authorized officer of Borrower (i) indicating its choice to pay a portion of its such interest in-kind and (ii) stating the amount of interest (not to exceed three percent (3%) per annum) that is being paid in-kind. [***]. All PIK Interest shall be payable when the principal amount of the Term Loan Advances are payable in accordance with Sections 2.1(d) and 2.3. Interest shall accrue on each Term Loan Advance commencing on, and including, the Advance Date of such Term Loan Advance (and, in the case of PIK Interest, as specified in the definition of PIK Interest), and shall accrue on the principal amount outstanding under such Term Loan Advance up to but not including the day on which such Term Loan Advance is paid in full.

(d) Payment. Borrower will pay interest on each Term Loan Advance on each Payment Date, beginning in each case on the Payment Date after the Advance Date for such Term Loan Advance and continuing until the Maturity Date. The entire outstanding principal balance of the Term Loan Advance and all accrued but unpaid interest hereunder shall be due and payable on the Maturity Date. Borrower shall make all payments under this Agreement without setoff, recoupment or deduction and regardless of any counterclaim or defense.

2.2 Maximum Interest. Notwithstanding any provision in this Agreement or any other Loan Document, it is the parties' intent not to contract for, charge or receive interest at a rate that is greater than the maximum rate permissible by law that a court of competent jurisdiction shall deem applicable hereto (which under the laws of the State of New York shall be deemed to be the laws relating to permissible rates of interest on commercial loans) (the "Maximum Rate"). If a court of competent jurisdiction shall finally determine that Borrower has actually paid to any Lender an amount of interest in excess of the amount that would have been payable if all of the Secured Obligations had at all times borne interest at the Maximum Rate, then such excess interest actually paid by Borrower shall be applied as follows: first, to the payment of the Secured Obligations consisting of the outstanding principal; second, after all principal is repaid, to the payment of such Lender's accrued interest, costs, expenses, professional fees and any other Secured Obligations; and third, after all Secured Obligations are repaid, the excess (if any) shall be refunded to Borrower.

2.3 Default Interest. In the event any payment is not paid on the scheduled payment date (except if due solely to an administrative or operational error of Administrative Agent or Lender or Borrower's bank if Borrower had the funds to make the payment when due), an amount equal to two percent (2%) of the past due amount shall be payable on demand. In addition, upon the occurrence and during the continuation of an Event of Default hereunder, all Secured Obligations, including principal (including PIK Interest added to the Term Loan Advances), interest, compounded interest, and professional fees, shall bear interest at a rate per annum equal to the rate set forth in Section 2.1(c), plus two percent (2%) per annum. In the event any interest is not paid when due hereunder, delinquent interest shall be added to principal and shall bear interest on interest, compounded at the rate set forth in Section 2.1(c) or Section 2.3, as applicable.

2.4 Prepayment.

(a) Optional Prepayment. At its option upon at least [***] Business Days prior written notice to Administrative Agent, Borrower may prepay all or a portion of the outstanding Advance by paying principal, and all accrued and unpaid interest thereon, together with a prepayment charge equal to the following percentage of the principal amount being prepaid: (i) if the prepayment is made prior to the first anniversary of the Closing Date, 3%, plus the Make-Whole Amount, (ii) if the prepayment is made on or after the first anniversary of the Closing Date and prior to the second anniversary of the Closing Date, 3%, (iii) if the prepayment is made on or after the second anniversary of the Closing Date and prior to the third anniversary of the Closing Date, 2%, (iv) if the prepayment is made on or after the third anniversary of the Closing Date and prior to the fourth anniversary of the Closing Date, 1%, and (v) if the prepayment is made on or after the fourth anniversary of the Closing Date, 0.0% (each, a "Prepayment Charge"), provided that each prepayment shall be in a minimum amount of $[***] or, if less, the remaining outstanding principal amount of the Advance. Borrower agrees that the Prepayment Charge is a reasonable calculation of Lender's lost profits in view of the difficulties and impracticality of determining actual damages resulting from an early repayment of the Advance or any portion thereof. Borrower shall prepay the outstanding amount of all principal and accrued interest through the prepayment date and the Prepayment Charge upon the occurrence of a Change in Control.

(b) Mandatory Prepayment.

(i) Within [***] Business Days of receipt of any Net Cash Proceeds from a Prepayment Event, Borrower shall prepay the outstanding Advance by paying up to (x) prior to the [***] Milestone Date, 75% of such Net Cash Proceeds and (y) from and after the [***] Milestone Date, 50% of such Net Cash Proceeds. For the avoidance of doubt, no Prepayment Charge shall apply to a prepayment in accordance with this Section 2.4(b).

(ii) [Reserved].

(c) Waivable Mandatory Prepayment. Anything contained herein to the contrary notwithstanding, in the event Borrower is required to make any mandatory prepayment pursuant to <u>Section 2.4(b)(i)</u> or <u>(ii)</u> (a "<u>Waivable Mandatory Prepayment</u>") of the Advances, by at least 1:00 p.m., New York Time not less than [***] Business Days prior to the date (the "<u>Required Prepayment Date</u>") on which Borrower is required to make such Waivable Mandatory Prepayment, Borrower shall notify Administrative Agent in writing (including by email) of the amount of such prepayment, and Administrative Agent will promptly thereafter notify each Lender holding any outstanding Advances of the amount of such Lender's pro rata share of such Waivable Mandatory Prepayment and such Lender's option to refuse such amount. Each such Lender may exercise such option by giving written notice to Borrower and Administrative Agent of its election to do so on or before 1:00 p.m., New York time, the [***] prior to the Required Prepayment Date (it being understood that any Lender which does not notify Borrower and Administrative Agent of its election to exercise such option on or before the [***] prior to the Required Prepayment Date shall be deemed to have elected, as of such date, not to exercise such option). On the Required Prepayment Date, Borrower shall pay to Administrative Agent the amount of the Waivable Mandatory Prepayment, which amount shall be applied (i) in an amount equal to that portion of the Waivable Mandatory Prepayment payable to those Lenders that have elected not to exercise such option, to prepay the Advances of such Lenders and (ii) to the extent of any excess as a result of any Lender that elected to exercise such option, to Borrower for working capital and general corporate purposes.

2.5 Fee Letters. Borrower shall pay (or cause to be paid) when due and payable under the terms of the Fee Letters to Agent and each Lender, as applicable, the fees set forth in the respective Fee Letters.

2.6 Notes. If so requested by a Lender by written notice to Borrower, then Borrower shall execute and deliver to such Lender (and/or, if applicable and if so specified in such notice, to any Person who is an assignee of such Lender pursuant to <u>Section 11.13</u>) (promptly after Borrower's receipt of such notice) a Term Note or Term Notes to evidence such Lender's Loans.

2.7 Pro Rata Treatment; Application of Payments. Subject to Section 2.4(c), each payment (including prepayment) on account of any fee and any reduction of the Term Loan Advance shall be made pro rata according to the aggregate outstanding Term Loan Advances of the Lenders (and on a pro rata basis as between the outstanding Tranche I Advances and Tranche II Advances). Each applicable Term Loan Advance shall be made pro rata according to the applicable Term Commitments of each relevant Lender. Any prepayment of the Term Loan Advances shall be applied to prepay the principal of the Term Loan Advances (on a pro rata basis as between the outstanding Tranche I Advances and Tranche II Advances) on a pro rata basis across all scheduled payments of Tranche I Advances and Tranche II Advances until paid in full.

2.8 Taxes.

(a) Withholding. Any and all payments by or on account of any obligation of any Loan Party under any Loan Document will be made free and clear of and without deduction or withholding for any Taxes, except as required by applicable law. If any applicable law (as determined in the good faith discretion of an applicable Withholding Agent) requires a Withholding Agent to make any deduction or withholding of any Tax from any such payment, then the applicable Withholding Agent shall be entitled to make such deduction or withholding and shall timely pay the full amount deducted or withheld to the relevant governmental authority in accordance with applicable law and, to the extent such Tax is an Indemnified Tax, then the sum payable by the applicable Loan Party shall be increased to the extent necessary to ensure that, after the making of such required deduction or withholding, Agent or Lender, as applicable receives an amount equal to the sum which it would have received had no such deduction or withholding been made. The applicable Loan Party will, upon request, furnish Agent with proof reasonably satisfactory to Agent indicating that such Loan Party has made such withholding payment.

(b) Payment of Other Taxes by the Loan Parties. The Loan Parties shall timely pay to the relevant governmental authority in accordance with applicable law, or at the option of Agent timely reimburse it for the payment of, any Other Taxes.

(c) Indemnification by the Loan Parties. The Loan Parties shall indemnify each Recipient, within [***] days after demand therefor, for the full amount of any Indemnified Taxes (including Indemnified Taxes imposed or asserted on or attributable to amounts payable under this Section) payable or paid by such Recipient or required to be withheld or deducted from a payment to such Recipient and any reasonable expenses arising therefrom or with respect thereto, whether or not such Indemnified Taxes were correctly or legally imposed or asserted by the relevant governmental authority; provided that the Loan Parties shall not be obligated to compensate any Recipient pursuant to this Section in respect of penalties, interest or other liabilities attributable to any Indemnified Taxes, if such penalties, interest and other liabilities result solely from the gross negligence or willful misconduct of such Lender, Agent or their Affiliates. A certificate as to the amount of such payment or liability delivered to Borrower by a Lender (with a copy to Agent), or by Agent on its own behalf or on behalf of a Lender, shall be conclusive absent manifest error.

(d) Status of Lender.

(i) Any Lender that is entitled to an exemption from or reduction of withholding Tax with respect to payments made under any Loan Document shall deliver to Borrower and Agent, at the time or times reasonably requested by Borrower or Agent, such properly completed and executed documentation reasonably requested by Borrower or Agent as will permit such payments to be made without withholding or at a reduced rate of withholding. In addition, any Lender, if reasonably requested by Borrower or Agent, shall deliver such other documentation prescribed by applicable law or reasonably requested by Borrower or Agent as will enable Borrower or Agent to determine whether or not such Lender is subject to backup withholding or information reporting requirements. Notwithstanding anything to the contrary in the preceding two sentences, the completion, execution and submission of such documentation (other than such documentation set forth in paragraphs (d)(ii)(A), (ii)(B) and (ii)(D) of this Section) shall not be required if in such Lender's reasonable judgment such completion, execution or submission would subject such Lender to any material unreimbursed cost or expense or would materially prejudice the legal or commercial position of such Lender.

(ii) Without limiting the generality of the foregoing,

(A) any Lender that is a U.S. Person shall deliver to Borrower and Agent on or about the date on which such Lender becomes a Lender under this Agreement (and from time to time thereafter upon the reasonable request of Borrower or Agent), executed copies of Internal Revenue Service ("IRS") Form W-9 certifying that such Lender is exempt from U.S. federal backup withholding tax;

(B) any Foreign Lender shall, to the extent it is legally entitled to do so, deliver to Borrower and Agent (in such number of copies as shall be requested by the recipient) on or about the date on which such Foreign Lender becomes a Lender under this Agreement (and from time to time thereafter upon the reasonable request of Borrower or Agent), whichever of the following is applicable:

(1) in the case of a Foreign Lender claiming the benefits of an income tax treaty to which the United States is a party (x) with respect to payments of interest under any Loan Document, executed copies of IRS Form W-8BEN or IRS Form W-8BEN-E establishing an exemption from, or reduction of, U.S. federal withholding Tax pursuant to the "interest" article of such tax treaty and (y) with respect to any other applicable payments under any Loan Document, IRS Form W-8BEN or IRS Form W-8BEN-E establishing an exemption from, or reduction of, U.S. federal withholding Tax pursuant to the "business profits" or "other income" article of such tax treaty;

(2) executed copies of IRS Form W-8ECI;

(3) in the case of a Foreign Lender claiming the benefits of the exemption for portfolio interest under Section 881(c) of the Code, (x) a certificate substantially in the form of Exhibit I-1 to the effect that such Foreign Lender is not a "bank" within the meaning of Section 881(c)(3)(A) of the Code, a "10 percent shareholder" of Borrower within the meaning of Section 871(h)(3)(B) of the Code, or a "controlled foreign corporation" related to Borrower as described in Section 881(c)(3)(C) of the Code (a "U.S. Tax Compliance Certificate") and (y) executed copies of IRS Form W-8BEN or IRS Form W-8BEN-E; or

(4) to the extent a Foreign Lender is not the beneficial owner, executed copies of IRS Form W-8IMY, accompanied by IRS Form W-8ECI, IRS Form W-8BEN, IRS Form W-8BEN-E, a U.S. Tax Compliance Certificate substantially in the form of Exhibit I-2 or Exhibit I-3, IRS Form W-9, and/or other certification documents from each beneficial owner, as applicable; provided that if the Foreign Lender is a partnership and one or more direct or indirect partners of such Foreign Lender are claiming the portfolio interest exemption, such Foreign Lender may provide a U.S. Tax Compliance Certificate

substantially in the form of Exhibit I-4 on behalf of each such direct and indirect partner;

(C) any Foreign Lender shall, to the extent it is legally entitled to do so, deliver to Borrower and Agent (in such number of copies as shall be requested by the recipient) on or about the date on which such Foreign Lender becomes a party to this Agreement (and from time to time thereafter upon the reasonable request of Borrower or Agent), executed copies of any other form prescribed by applicable law as a basis for claiming exemption from or a reduction in U.S. federal withholding Tax, duly completed, together with such supplementary documentation as may be prescribed by applicable law to permit Borrower or Agent to determine the withholding or deduction required to be made; and

(D) if a payment made to a Lender under any Loan Document would be subject to U.S. federal withholding Tax imposed by FATCA if such Lender were to fail to comply with the applicable reporting requirements of FATCA (including those contained in Section 1471(b) or 1472(b) of the Code, as applicable), such Lender shall deliver to Borrower and Agent at the time or times prescribed by law and at such time or times reasonably requested by Borrower or Agent such documentation prescribed by applicable law (including as prescribed by Section 1471(b)(3)(C)(i) of the Code) and such additional documentation reasonably requested by Borrower or Agent as may be necessary for Borrower and Agent to comply with their obligations under FATCA and to determine that such Lender has complied with such Lender's obligations under FATCA or to determine the amount, if any, to deduct and withhold from such payment. Solely for purposes of this clause (D), "FATCA" shall include any amendments made to FATCA after the date of this Agreement.

Each Lender agrees that if any form or certification it previously delivered expires or becomes obsolete or inaccurate in any respect, it shall update such form or certification or promptly notify Borrower and Agent in writing of its legal inability to do so.

(e) Treatment of Certain Refunds. If any party determines, in its sole discretion exercised in good faith, that it has received a refund of any Taxes as to which it has been indemnified pursuant to this Section (including by the payment of additional amounts pursuant to this Section), it shall pay to the indemnifying party an amount equal to such refund (but only to the extent of indemnity payments made under this Section with respect to the Taxes giving rise to such refund), net of all out-of-pocket expenses (including Taxes) of such indemnified party and without interest (other than any interest paid by the relevant governmental authority with respect to such refund). Such indemnifying party, upon the request of such indemnified party, shall repay to such indemnified party the amount paid over pursuant to this paragraph (e) (plus any penalties, interest or other charges imposed by the relevant governmental authority) in the event that such indemnified party is required to repay such refund to such governmental authority. Notwithstanding anything to the contrary in this paragraph (e), in no event will the indemnified party be required to pay any amount to an indemnifying party pursuant to this paragraph (e) the payment of which would place the indemnified party in a less favorable net after-Tax position than the indemnified party would have been in if the Tax subject to indemnification and giving rise to such refund had not been deducted, withheld or otherwise imposed and the indemnification payments or additional amounts with respect to such Tax had never been paid. This paragraph shall not be construed to require any indemnified party to make available its Tax returns (or any other information relating to its Taxes that it deems confidential) to the indemnifying party or any other Person.

(f) Survival. Each party's obligations under this Section shall survive the resignation or replacement of Agent or any assignment of rights by, or the replacement of, a Lender, the termination of the Term Commitments and the repayment, satisfaction or discharge of all obligations under any Loan Document.

2.9 Treatment of Prepayment Charge. It is understood and agreed that if the Loans are accelerated or otherwise become due prior to the Maturity Date, including without limitation as a result of any Event of Default set forth in Section 9.5 (including the acceleration of claims by operation of law), the Prepayment Charge that would have been payable if the Loans were optionally prepaid pursuant to Section 2.4(a) on such date of acceleration will also automatically be due and payable and shall constitute part of the Secured Obligations with respect to the Loans, in view of the impracticability and extreme difficulty of ascertaining actual damages and by mutual agreement of the parties as to a reasonable calculation of each Lender's lost profits as a result thereof. Any such Prepayment Charge payable shall be presumed to be the liquidated damages sustained by each Lender as the result of the early prepayment and each of the Loan Parties agrees that it is reasonable under the circumstances currently existing. The Prepayment Charge shall also be payable in the event the Secured Obligations (and/or this Agreement) are satisfied or released by foreclosure (whether by power of judicial proceeding), deed in lieu of foreclosure, or by any other means. BORROWER EXPRESSLY WAIVES (TO THE FULLEST EXTENT IT MAY LAWFULLY DO SO) THE PROVISIONS OF ANY PRESENT OR FUTURE STATUTE OR LAW THAT PROHIBITS OR MAY PROHIBIT THE COLLECTION OF THE FOREGOING PREPAYMENT CHARGE IN CONNECTION WITH ANY SUCH ACCELERATION. Each Loan Party agrees (to the fullest extent that each may lawfully do so): (a) the Prepayment Charge is reasonable and is the product of an arm's length transaction between sophisticated business people, ably represented by counsel; (b) the Prepayment Charge shall be payable notwithstanding the then prevailing market rates at the time payment is made; (c) there has been a course of conduct between Lender and Borrower giving specific consideration in this transaction for such agreement to pay the Prepayment Charge as a charge (and not interest) in the event of repayment, prepayment or acceleration; and (d) The Loan Parties shall be estopped from claiming differently than as agreed to in this paragraph. The Loan Parties expressly acknowledges that their agreement to pay the Prepayment Charge to each Lender as herein described was on the Closing Date and continues to be a material inducement to each Lender to provide the Term Loan Advances.

2.10 Termination and Reduction of Commitments.

(a) The Tranche I Term Commitments shall automatically terminate upon the making of the Tranche I Advance on the Closing Date.

(b) The Tranche II Term Commitments shall automatically terminate (x) on a dollar-for-dollar basis upon the making of any Tranche II Advance on the applicable Advance Date and (y) if not previously terminated, in full on the Delayed Draw Expiration Date.

(c) Upon at least [***] Business Days' prior revocable written notice to Administrative Agent, Borrower may at any time in whole permanently terminate, or from time to time in part permanently reduce, the Tranche II Term Commitments; provided that each partial reduction of the Term Commitments shall be in an integral multiple of $[***] and in a minimum amount of $[***].

(d) Each reduction in the Tranche II Term Commitments shall be made ratably among the Lenders in accordance with their respective applicable Tranche II Term Commitments.

(e) Borrower, so long as no Default or Event of Default has occurred and is continuing, may terminate any Term Loan Commitment of any Defaulting Lender upon the prior notice of not less than [***] to the Agent, and in such event the payment waterfall provisions of Section 2.11(a)(ii) shall apply to all amounts thereafter paid by the Borrower for the account of such Defaulting Lender under this Agreement (whether on account of principal, interest, fees or other amounts); *provided*, that such termination shall not be deemed to be a waiver or release of any claim the Borrower, the Agent or any Lender may have against such Defaulting Lender.

2.11 Defaulting Lenders.

(a) Defaulting Lender Adjustments. Notwithstanding anything to the contrary contained in this Agreement, if any Lender becomes a Defaulting Lender, then, until such time as such Lender is no longer a Defaulting Lender, to the extent permitted by applicable law:

(i) Waivers and Amendments. Such Defaulting Lender's right to approve or disapprove any amendment, waiver or consent with respect to this Agreement shall be restricted as set forth in the definition of Required Lenders and Section 11.3(b).

(ii) Defaulting Lender Waterfall. Any payment of principal, interest, fees or other amounts received by the Agent for the account of such Defaulting Lender (whether voluntary or mandatory, at maturity or otherwise) shall be applied at such time or times as may be determined by the Agent in the following order of priority: *first*, to the payment of any amounts owing by such Defaulting Lender to the Agent hereunder; *second*, as Borrower may request (so long as no Default or Event of Default exists), to the funding of any Loan in respect of which such Defaulting Lender has failed to fund its portion thereof as required by this Agreement, as determined by the Agent; *third*, if so determined by the Agent and Borrower, to be held in a deposit account and released pro rata in order to satisfy such Defaulting Lender's potential future funding obligations with respect to Loans under this Agreement; *fourth*, to the payment of any amounts owing to the Lenders as a result of any judgment of a court of competent jurisdiction obtained by any Lender against such Defaulting Lender as a result of such Defaulting Lender's breach of its obligations under this Agreement; *fifth*, so long as no Default or Event of Default exists, to the payment of any amounts owing to Borrower as a result of any judgment of a court of competent jurisdiction obtained by Borrower against such Defaulting Lender as a result of such Defaulting Lender's breach of its obligations under this Agreement; and *sixth*, to such Defaulting Lender or as otherwise directed by a court of competent jurisdiction; provided that if (x) such payment is a payment of the principal amount of any Loans in respect of which such Defaulting Lender has not fully funded its appropriate share, and (y) such Loans were made at a time when the applicable conditions set forth in Section 4 were satisfied or waived, such payment shall be applied solely to pay the Loans of all Non-Defaulting Lenders on a pro rata basis prior to being applied to the payment of any Loans of such Defaulting Lender until such time as all Loans are held by the Lenders pro rata in accordance with the Term Commitments. Any payments, prepayments or other amounts paid or payable to a Defaulting Lender that are applied (or held) to pay amounts owed by a Defaulting Lender pursuant to this Section shall be deemed paid to and redirected by such Defaulting Lender, and each Lender irrevocably consents hereto.

(iii) Fees. No Defaulting Lender shall be entitled to receive any fees for any period during which that Lender is a Defaulting Lender (and the Borrower shall not be required to pay any such fee that otherwise would have been required to have been paid to that Defaulting Lender), other than as specified in the Fee Letter.

(b) Defaulting Lender Cure. If the Borrower and the Agent agree in writing that a Lender is no longer a Defaulting Lender, the Agent will so notify the parties hereto, whereupon as of the effective date specified in such notice and subject to any conditions set forth therein, that such Lender will, to the extent applicable, purchase at par that portion of outstanding Loans of the other Lenders or take such other actions as the Agent may determine to be necessary to cause the Loans to be held pro rata by the Lenders in accordance with the Term Loan Commitments whereupon, such Lender will cease to be a Defaulting Lender; provided that no adjustments will be made retroactively with respect to fees accrued or payments made by or on behalf of the Borrower while that such Lender was a Defaulting Lender; and provided, further, that except to the extent otherwise expressly agreed by the affected parties, no change hereunder from Defaulting Lender to such Lender will constitute a waiver or release of any claim of any party hereunder arising from that Lender's having been a Defaulting Lender.

SECTION 3.SECURITY INTEREST

3.1 Grant of Security Interest. As security for the prompt and complete payment when due (whether on the payment dates or otherwise) of all the Secured Obligations, each Loan Party grants to the Collateral Agent for the benefit of the Secured Parties a security interest in all of such Loan Party's right, title, and interest in, to and under all of such Loan Party's personal property and other assets including without limitation the following (except as set forth herein) whether now owned or hereafter acquired (collectively, the "Collateral"): (a) Receivables; (b) Equipment; (c) Fixtures; (d) General Intangibles; (e) Inventory; (f) Investment Property; (g) Deposit Accounts; (h) Cash; (i) Goods; (j) Intellectual Property; and all other tangible and intangible personal property of such Loan Party whether now or hereafter owned or existing, leased, consigned by or to, or acquired by, such Loan Party and wherever located, and any of such Loan Party's property in the possession or under the control of the Collateral Agent; and, to the extent not otherwise included, all Proceeds of each of the foregoing and all accessions to, substitutions and replacements for, and rents, profits and products of each of the foregoing.

3.2 Excluded Collateral. Notwithstanding the broad grant of the security interest set forth in Section 3.1, above, the Collateral shall not include (a) non-assignable licenses or contracts, which by their terms require the consent of the licensor thereof or another party (but only to the extent such prohibition on transfer is enforceable under applicable law, including, without limitation, Sections 9-406, 9-407 and 9-408 of the UCC) or Pledged Collateral consisting of Equity Interests, if pursuant to the terms of the applicable Equity Documents, a pledge of such Equity Interests would be prohibited or void or would require the consent of or waiver by the applicable Platform Company (or, in the case of LianBio, applicable counterparties) other than, in any case, any Loan Party, provided further, that upon the lapse of such prohibition or such consent or waiver being provided with respect to any license or contract, such license, contract or Equity Interests shall automatically be included in the Collateral, (b) any property which is subject to a capital lease, purchase money Lien or similar equipment financing permitted under this Agreement, but only to the extent and for as long as a Lien in favor of the Collateral Agent would be prohibited by the terms of the related equipment financing agreement or would result in a termination thereof, and provided further, that upon the termination of such prohibition, such property shall automatically be deemed included in the Collateral, (c) any trademark application filed on an "intent-to-use" basis until the earlier of the filing of a statement of use with respect thereto or the issuance of a registration therefor, and (d) Excluded Accounts.

3.3 Pledged Collateral.

(a) Each Loan Party hereby pledges, collaterally assigns and grants to the Collateral Agent for the benefit of the Secured Parties a security interest in the Pledged Collateral, as security for the performance of the Secured Obligations. Each Loan Party irrevocably waives any and all of its rights under provisions of any Organizational Documents of any Subsidiary which is a limited liability company or limited partnership, and under the laws under which such Subsidiary has been organized, to the extent such Loan Party has the legal capacity to do so and that such waiver is permitted, that would operate to (a) prohibit, restrict, condition or otherwise adversely affect the pledge hereunder or any enforcement action which may be taken in respect of this pledge or (b) otherwise conflict with the terms of this Section 3.3. Each Loan Party of which Equity Interests consisting of limited liability company or limited partnership interests constitute Pledged Collateral hereby irrevocably consents to the grant of the security interest provided for herein and to the Collateral Agent or its nominee becoming a member or limited or general partner, as applicable, in such limited liability company or limited partnership, as applicable (including succeeding to any management rights appurtenant thereto), in connection with the exercise of remedies pursuant to Section 10; provided that such successor member or partner, as applicable, then agrees in writing to be bound by, and a party to, the applicable Organizational Document pursuant to the terms therein.

(b) Except as otherwise expressly provided in this Agreement, any sums or other property paid or distributed upon or with respect to any of the Pledged Collateral, whether by dividend or redemption or upon the liquidation or dissolution or recapitalization or reclassification of the capital of any issuer of the applicable Equity Interests or otherwise, shall, be paid over and delivered to the Collateral Agent to be held by the Collateral Agent as security for the payment in full in Cash of all of the Secured Obligations, in each case, to the extent constituting Net Cash Proceeds. All payments received by a Loan Party shall, until paid or delivered to the Collateral Agent, be held in trust for the Collateral Agent, as security for the payment and performance in full of all of the Secured Obligations, and when paid, shall be deposited into a Controlled Account.

(c) So long as no Event of Default shall have occurred and be continuing and at the Collateral Agent's written direction to the contrary, each Loan Party shall be entitled to receive all cash dividends and distributions paid in respect of Pledged Collateral owned by it, and, prior to any acceleration pursuant to Section 10.1 hereof and any election by the Collateral Agent of any remedies pursuant to Section 10.2 hereof, each Loan Party shall be entitled to vote any Equity Interests owned by it and to give consents, waivers and ratifications in respect of Pledged Collateral; provided, however, that no vote shall be cast or consent, waiver or ratification given by any Loan Party if the effect thereof would materially impair the Collateral Agent's rights with respect to the enforcement of its Lien on the Pledged Collateral or be inconsistent with or result in any violation of any of the provisions of this Agreement or any of the Loan Documents. All rights of any Loan Party to receive cash dividends and distributions with respect to Pledged Collateral owned by such Loan Party, and, at the Collateral Agent's option, upon notice by the Collateral Agent to the applicable Loan Party, all right to vote and give consents, waivers and ratifications with respect to such Pledged Collateral, shall terminate upon the occurrence and during the continuation of an Event of Default.

3.4 Release; Agreements by Collateral Agent with respect to Pledged Collateral.

The security interest granted pursuant to this Agreement shall be automatically released (a) with respect to all Collateral upon the payment in full in Cash of all Secured Obligations in accordance with this Agreement (other than contingent indemnity obligations for which no claim is outstanding), (b) with respect to any Pledged Collateral that is the subject of a sale or other Disposition that constitutes a “Permitted Transfers” and is otherwise permitted hereunder as certified to the Collateral Agent by Borrower as being permitted hereunder, upon the consummation of such transaction, or (c) if otherwise approved, authorized or ratified in writing by the Required Lenders in their discretion. Upon such release, the Collateral Agent shall, upon the reasonable request and at the sole cost and expense of the Loan Parties, assign, transfer and deliver to the Loan Parties, against receipt and without recourse to or warranty by the Collateral Agent, except as to the fact that the Collateral Agent does not continue to encumber the released assets, such Collateral or any part thereof, which shall be released in accordance with customary documents and instruments (including UCC-3 termination financing statements or releases) acknowledging the release of such Collateral. The Collateral Agent agrees, on behalf of itself and the Lenders, that if any Platform Company is consummating an initial public offering of its stock or any relevant follow on offering that is certified to the Collateral Agent by Borrower as being a permitted transaction hereunder, that Agent shall enter into lockup or similar agreements (in form and substance reasonably satisfactory to the Required Lenders) reasonably requested by any Loan Party or any underwriter with respect to the Collateral Agent’s exercise of remedies with respect to the Pledged Collateral constituting Equity Interests the Platform Company that is the issuer in such offering, in each case at the sole cost and expense of the Loan Parties.

SECTION 4.CONDITIONS PRECEDENT TO LOAN

The obligations of each Lender to make the applicable Loans hereunder are subject to the satisfaction by Borrower of the following conditions:

4.1 Initial Advance. On or prior to the Closing Date, Borrower shall have delivered to the Lenders and Agents the following:

(a) duly executed copies of the following, in form and substance acceptable to Lenders and ~~Agents:~~

Agents:

(i) this Agreement;

(ii) Account Control Agreements with respect to all Deposit Accounts and any accounts where Investment Property is maintained, as required by Section 7.12 hereof, including the Account Control Agreements set forth on Schedule 4.1;

(iii) a duly executed certificate of an officer of each Loan Party certifying and attaching copies of (A) the Charter, certified as of a recent date by the jurisdiction of organization of such Loan Party as in effect as of the Closing Date; (B) the bylaws, operating agreement or similar governing document of such Loan Party, as in effect as of the Closing Date; (C) resolutions of such Loan Party’s Board (or similar governing body) evidencing approval of the Loan and other transactions contemplated by the Loan Documents, as in effect as of the Closing Date; (D) resolutions of the holders of such Loan Party’s Equity Interests in connection with the transactions contemplated by this Agreement as in effect as of the Closing Date, to the extent required by the applicable

Organizational Documents; and (E) a schedule setting forth the name, title and specimen signature of officers or other authorized signers on behalf of each Loan Party;

(iv) a duly executed certificate of an officer of Borrower certifying and attaching copies of (A) the Charter, certified as of a recent date by the jurisdiction of organization of each Platform Company, as in effect as of the Closing Date; (B) the bylaws, operating agreement or similar governing document of each Platform Company; (C) copies of all Equity Documents in effect as of the Closing Date; and (D) a summary capitalization table of each Platform Company;

(v) a legal opinion of Borrower's counsel;

(vi) any other Loan Documents; and

(vii) all other documents and instruments reasonably required by Lenders or Agents to effectuate the transactions contemplated hereby or to create and perfect the Liens of Collateral Agent with respect to all Collateral.

(b) all originals certificates evidencing Pledged Collateral pledged pursuant to Section 3.3, together with any transfer powers or other instruments of transfer, in form and substance acceptable to Lenders;

(c) copies of all consents, waivers, notices and other documents set forth on Schedule 5.15(ii);

(d) a certificate of good standing for each Loan Party from its jurisdiction of organization;

(e) payment of any fees due and payable under the Fee Letters and reimbursement of Agent's and each Lender's current expenses reimbursable pursuant to this Agreement, which amounts may be deducted from the initial Advance;

(f) all certificates of insurance, endorsements, and copies of each insurance policy required pursuant to Section 6.2;

(g) the Refinancing shall have been or, substantially concurrently with the initial Advance hereunder, shall be consummated;

(h) the Lenders will have received all documentation and other information required by bank regulatory authorities under applicable "know-your-customer" and anti-money laundering rules and regulations including the PATRIOT Act at least [***] Business Days prior to the Closing Date, to the extent requested from the Borrower, at least [***] Business Days prior to the Closing Date; and

(i) such other documents as Lenders or Agents may reasonably request (which documents shall include the Perfection Certificate).

Notwithstanding the foregoing, to the extent any of the above closing conditions is set forth on Schedule 7.19, Borrower may deliver the same when required to be delivered pursuant to Schedule 7.19.

4.2 All Advances. On the Advance Date:

(a) Administrative Agent shall have received (i) an Advance Request for the relevant Advance as required by Section 2.1(b), duly executed by Borrower's Chief Executive Officer or Chief Financial Officer, and (ii) any other documents Agent or Lender may reasonably request.

(b) Agents and Lenders shall have received the applicable fees due and payable under the Fee Letters with respect to such Advance.

(c) The representations and warranties set forth in this Agreement shall be true and correct in all material respects (or, to the extent any such representation or warranty is qualified by any applicable standard of materiality, in all respects) on and as of the Advance Date with the same effect as though made on and as of such date, except to the extent such representations and warranties expressly relate to an earlier date.

(d) At the time of and immediately after such Advance, no Default or Event of Default shall have occurred and be continuing.

(e) Each Advance Request shall be deemed to constitute a representation and warranty by Borrower on the relevant Advance Date as to the matters specified in subsections (b) and (c) of this Section 4.2 and as to the matters set forth in the Advance Request.

(f) In the case of Tranche II Advances requested pursuant to Section 2.1(a)(ii), [***], and Borrower shall certify in the applicable Advance Request that [***] and certify that [***].

4.3 No Default. As of the Closing Date and each Advance Date, (i) no fact or condition exists that could constitute a Default or an Event of Default and (ii) no event that has had or could reasonably be expected to have a Material Adverse Effect has occurred and is continuing.

SECTION 5. REPRESENTATIONS AND WARRANTIES OF THE LOAN PARTIES

Each Loan Party represents and warrants that:

5.1 Organizational Status. Each Loan Party is duly organized, legally existing and in good standing under the laws of its jurisdiction of organization, and is duly qualified as a foreign corporation, limited liability company or partnership, as the case may be, in all jurisdictions in which the nature of its business or location of its properties requires such qualifications and where the failure to be qualified could reasonably be expected to have a Material Adverse Effect. Each Loan Party's present name, former names (if any), locations, place of formation, tax identification number, organizational identification number and other information are correctly set forth in Exhibit C, or as such Loan Party has subsequently notified Agent after the Closing Date in accordance with this Agreement (including in any Compliance Certificate).

5.2 Collateral. Each Loan Party owns the Collateral free of all Liens, except for Permitted Liens. Each Loan Party has the power and authority to grant to Collateral Agent a Lien in the Collateral as security for the Secured Obligations.

5.3 Consents. Each Loan Party's execution, delivery and performance of this Agreement and all other Loan Documents, (i) have been duly authorized by all necessary action in accordance with such Loan Party's Organizational Documents, (ii) will not result in the creation or imposition of any Lien upon the Collateral, other than Permitted Liens and the Liens created by this Agreement and the other Loan Documents, (iii) do not violate any provisions of (A) such Loan Party's Organizational Documents, or (B) any, law, regulation, order, injunction, judgment, decree or writ to which such Loan Party is subject and which violation would have a Material Adverse Effect and (iv) do not violate any contract or agreement or require the consent or approval of any other Person which has not already been obtained if such violation or failure to obtain consent or approval would have a Material Adverse Effect. The individual or individuals executing the Loan Documents are duly authorized to do so.

5.4 Material Adverse Effect. Since the Closing Date, no event that has had or would reasonably be expected to have a Material Adverse Effect has occurred and is continuing.

5.5 Actions Before Governmental Authorities. There are no actions, suits or proceedings at law or in equity or by or before any governmental authority now pending or, to the knowledge of any Loan Party, threatened against or affecting any Loan Party or its property, that is reasonably expected to result in a Material Adverse Effect.

5.6 Laws.

(a) Neither any Loan Party nor any of its Subsidiaries is in violation of any law, rule or regulation, or in default with respect to any judgment, writ, injunction or decree of any governmental authority, where such violation or default is reasonably expected to result in a Material Adverse Effect. No Loan Party is in default in any material respect in any manner under any provision of any agreement or instrument evidencing material Indebtedness, or any other material agreement to which it is a party or by which it is bound.

(b) No Loan Party is required to be registered as an "investment company" within the meaning of the Investment Company Act based on (i) Section 3(a)(1)(C) of the Investment Company Act, (ii) Rule 3a-1 promulgated under the Investment Company Act or (iii) certain other exemptions or exceptions from registration under the Investment Company Act, other than Sections 3(c)(1) or 3(c)(7) of the Investment Company Act. No Loan Party nor any of its Subsidiaries (other than BB Square Capital) is engaged as one of its important activities in the business of purchasing or carrying margin stock, or extending credit for margin stock (under Regulations X, T and U of the Federal Reserve Board of Governors). No part of the proceeds of any Term Loan Advance will be used, whether directly or indirectly, and whether immediately, incidentally or ultimately, for purchasing or carrying margin stock or for any other purpose that entails a violation of, or that is inconsistent with, the provisions of the regulations of the Federal Reserve Board of Governors, including Regulation X, T and U. Each Loan Party with activities in the United States has complied in all material respects with the Federal Fair Labor Standards Act. No Loan Party nor any of its Subsidiaries a "holding company" or an "affiliate" of a "holding company" or a "subsidiary company" of a "holding company" as each term is defined and used in the Public Utility Holding Company Act of 2005. No Loan Party's nor any of its Subsidiaries' properties or assets has been used by any Loan Party or such Subsidiary or, to any Loan Party's knowledge, by previous Persons, in disposing, producing, storing, treating, or transporting any hazardous substance other than in material compliance with applicable laws. Each Loan Party and each of its Subsidiaries has obtained all consents, approvals and authorizations of, made all declarations or filings with, and given all notices to, all governmental authorities that are necessary to continue their respective businesses as currently conducted.

(c) No Loan Party, any of its Subsidiaries or, to any Loan Party's knowledge, any of its or its Subsidiaries' Affiliates or any of their respective agents acting or benefiting in any capacity in connection with the transactions contemplated by this Agreement is (i) in violation of any Anti-Terrorism Law, (ii) engaging in or conspiring to engage in any transaction that evades or avoids, or has the purpose of evading or avoiding or attempts to violate, any of the prohibitions set forth in any Anti-Terrorism Law, or (iii) is a Blocked Person. No Loan Party nor any of its Subsidiaries, or to the knowledge of any Loan Party, any of their Affiliates or agents, acting or benefiting in any capacity in connection with the transactions contemplated by this Agreement, (x) conducts any business or engages in making or receiving any contribution of funds, goods or services to or for the benefit of any Blocked Person, or (y) deals in, or otherwise engages in any transaction relating to, any property or interest in property blocked pursuant to Executive Order No. 13224, any similar executive order or other Anti-Terrorism Law. None of the funds to be provided under this Agreement will be used, directly or indirectly, (a) for any activities in violation of any applicable anti-money laundering, economic sanctions and anti-bribery laws and regulations laws and regulations or (b) for any payment to any governmental official or employee, political party, official of a political party, candidate for political office, or anyone else acting in an official capacity, in order to obtain, retain or direct business or obtain any improper advantage, in violation of the United States Foreign Corrupt Practices Act of 1977, as amended.

5.7 Information Correct and Current. No information, report, Advance Request, financial statement, exhibit or schedule furnished, by or on behalf of any Loan Party to Agent or the Lenders in connection with any Loan Document or included therein or delivered pursuant thereto contained, or, when taken as a whole, contains or will contain any material misstatement of fact or, when taken together with all other such information or documents, omitted, omits or will omit to state any material fact necessary to make the statements therein, in the light of the circumstances under which they were, are or will be made, not materially misleading at the time such statement was made or deemed made. Additionally, any and all financial or business projections provided by the Loan Parties to Agent or the Lenders, whether prior to or after the Closing Date, shall be (i) provided in good faith and based on the most current data and information available to the Loan Parties, and (ii) the most current of such projections provided to Borrower’s Board, provided that it is understood that the projections are based on assumptions made in good faith but are subject to significant uncertainties and contingencies and that actual results may differ significantly and no assurances are provided by any Loan Party for any projections made or given.

5.8 Tax Matters. Except to the extent contested in good faith with adequate reserves under GAAP, (a) each Loan Party has filed all material federal and state income tax returns and other tax returns that it is required to file, (b) each Loan Party has duly paid or fully reserved for all federal and state income Taxes and other material Taxes or installments thereof (including any interest or penalties) as and when due, which have or may become due pursuant to such returns, and (c) each Loan Party has paid or fully reserved for any material Tax assessment received by such Loan Party for the three (3) years preceding the Closing Date, if any (including any material Taxes being contested in good faith and by appropriate proceedings).

5.9 Intellectual Property Claims. To the Loan Parties’ knowledge, each Platform Company is the sole owner of, or otherwise has the right to use, the Intellectual Property material to such Platform Company’s business. To the Loan Parties’ knowledge, each of the material Copyrights, Trademarks and Patents is valid and enforceable, no material part of the Intellectual Property of a Platform Company has been judged invalid or unenforceable, in whole or in part, and no claim has been made to a Loan Party or, to the Loan Parties’ knowledge, to a Platform Company, that any material part of the Intellectual Property of a Platform Company violates the rights of any third party. Exhibit D is a true, correct and complete list of all Trademarks, Copyrights, Patents and mask works of each Loan Party, together with application or registration numbers, as applicable, and of all material agreements under which a Loan Party or Platform Company licenses Intellectual Property from third parties (other than shrink-wrap software licenses or software licenses available in the ordinary course of business), in each case as of the Closing Date. No Loan Party, or, to the Loan Parties' knowledge, no Platform Company is in material breach of, nor has such Person failed to perform any material obligations under, any material contracts, licenses or agreements and, to the Loan Parties' knowledge, no third party to any such contract, license or agreement is in material breach thereof or has failed to perform any material obligations thereunder.

5.10 Intellectual Property. To the Loan Parties' knowledge, each Platform Company has all material rights with respect to Intellectual Property necessary or material in the operation or conduct of such Person's business as currently conducted and proposed to be conducted. Without limiting the generality of the foregoing, and in the case of licenses, except for restrictions that are unenforceable under Division 9 of the UCC, to the Loan Parties' knowledge, each Platform Company has the right, to the extent required to operate such Platform Company's business, to freely transfer, license or assign Intellectual Property necessary or material in the operation or conduct of such Platform Company's business as currently conducted and proposed to be conducted, without condition, restriction or payment of any kind (other than license payments in the ordinary course of business) to any third party, and, to the Loan Parties' knowledge, each Platform Company owns or has the right to use, pursuant to valid licenses, all software development tools, library functions, compilers and all other third-party software and other items that are material to such Platform Company's business and used in the design, development, promotion, sale, license, manufacture, import, export, use or distribution of Products except customary covenants in inbound license agreements and equipment leases where a Platform Company is the licensee or lessee.

5.11 Products. No Material Intellectual Property owned by a Loan Party, or, to the Loan Parties' knowledge, Platform Company or Product has been or is subject to any actual or, to the knowledge of any Loan Party, threatened litigation, proceeding (including any proceeding in the United States Patent and Trademark Office or any corresponding foreign office or agency) or outstanding decree, order, judgment, settlement agreement or stipulation that restricts in any manner the use, transfer or licensing thereof by the owner thereof or that may affect the validity, use or enforceability thereof. There is no decree, order, judgment, agreement, stipulation, arbitral award or other provision entered into in connection with any litigation or proceeding that obligates any Loan Party, or, to the Loan Parties' knowledge, Platform Company to grant licenses or ownership interest in any future Material Intellectual Property related to the operation or conduct of the business of any Loan Party, or Platform Company or to any Products. Except as disclosed on Schedule 5.11, no Loan Party or, to the Loan Parties' knowledge, Platform Company has received any written notice or claim, or, to the knowledge of any Loan Party, oral notice or claim, challenging or questioning any Loan Party's, or Platform Company's ownership in any Material Intellectual Property (or written notice of any claim challenging or questioning the ownership in any licensed Intellectual Property of the owner thereof) or suggesting that any third party has any claim of legal or beneficial ownership with respect thereto nor, to the Loan Parties' knowledge, is there a reasonable basis for any such claim. Neither any use by any Loan Party, or, to the Loan Parties' knowledge, by Platform Company, of its respective Material Intellectual Property nor the production and sale of Products infringes in any material respect on the Intellectual Property or other rights of others.

5.12 Financial Accounts. Exhibit E, as may be updated by the Loan Parties in a written notice provided to Agent after the Closing Date, is a true, correct and complete list of (a) all banks and other financial institutions at which any Loan Party maintains Deposit Accounts and

(b) all institutions at which any Loan Party maintains an account holding Investment Property, and such exhibit correctly identifies the name and address of each bank or other institution, the name in which the account is held, a description of the purpose of the account, and the complete account number therefor.

5.13 Employee Loans. Other than loans constituting Permitted Investments, no Loan Party has any outstanding loans to any employee, officer, manager or director of such Loan Party, nor has any Loan Party guaranteed the payment of any loan made to an employee, officer, manager or director of such Loan Party by a third party.

5.14 Capitalization and Subsidiaries. Except as set forth on Schedule 5.14, as of the Closing Date, no Equity Interests of a Platform Company are owned by any Loan Party indirectly through a Subsidiary of such Loan Party. No Loan Party owns any stock, partnership interest or other securities of any Person, except for Permitted Investments.

5.15 Pledged Collateral; Instruments. All Equity Interests constituting Pledged Collateral are validly issued, fully paid and non-assessable in all material respects. The execution, delivery and performance thereof and the pledge of and granting of a security interest in the Pledged Collateral under this Agreement do not contravene any provision of the Organizational Documents of the issuer of such Equity Interests. All certificates representing any Loan Party's interest in Pledged Collateral have been delivered to Agent, together with duly executed transfer powers or other appropriate instruments of transfer (each in form and substance satisfactory to Lenders), duly executed in blank by the applicable Loan Party. As of the Closing Date, Schedule 5.15 sets forth (i) a true and accurate schedule of all Pledged Collateral and all Instruments owned by the Loan Parties, and (ii) a complete and accurate list of all consents, waivers, amendment or modification or other action to be taken in connection with the grant of the security interest pursuant to the terms of this Agreement in the Pledged Collateral.

5.16 Foreign Subsidiary or Foreign Subsidiary Holdco. No decision or action in any governing document of any Foreign Subsidiary or Foreign Subsidiary Holdco requires a vote of greater than 50.1% of the Equity Interests or voting rights of such Subsidiary.

SECTION 6. INSURANCE; INDEMNIFICATION

6.1 Coverage. The Loan Parties shall cause to be carried and maintained commercial general liability insurance, on an occurrence form, against risks customarily insured against in the Loan Parties' line of business. Such risks shall include the risks of bodily injury, including death, property damage, personal injury, advertising injury, and contractual liability per the terms of the indemnification agreement found in Section 6.3. The Loan Parties must maintain a minimum of $[***] of commercial general liability insurance for each occurrence. The Loan Parties have and agree to maintain a minimum of $[***] of directors' and officers' insurance for each occurrence and $[***] in the aggregate. So long as there are any Secured Obligations outstanding, the Loan Parties shall also cause to be carried and maintained insurance upon the business and assets of the Loan Parties and each of their Subsidiaries, insuring against all risks of physical loss or damage howsoever caused, in an amount not less than the full replacement cost of the Collateral, provided that such insurance may be subject to standard exceptions and deductibles.

6.2 Certificates. The Loan Parties shall deliver to Agent certificates of insurance that evidence their compliance with its insurance obligations in Section 6.1 and the obligations contained in this Section 6.2. The Loan Parties' insurance certificate shall state Agent (shown as "U.S. Bank National Association (and its permitted successors and assigns)", as "Collateral

Agent") is an additional insured for commercial general liability, a lender loss payee for all risk property damage insurance, subject to the insurer's approval, and promptly following any purchase of new or replacement insurance, the Loan Parties shall deliver to Agent certificates of insurance showing Agent as additional insured and a lender loss payee for property insurance and additional insured for liability insurance for any future insurance that the Loan Parties may acquire from such insurer. Attached to the certificates of insurance will be additional insured endorsements for liability and lender's loss payable endorsements for all risk property damage insurance. All certificates of insurance will provide for a minimum of [***] days advance written notice to Agent of cancellation (other than cancellation for non-payment of premiums, for which [***] days' advance written notice shall be sufficient) or any other change adverse to Agent's interests. Any failure of Agent to scrutinize such insurance certificates for compliance is not a waiver of any of Agent's rights, all of which are reserved. At Agent's reasonable request (as directed by the Required Lenders), the Loan Parties shall provide Agent with copies of each insurance policy, and upon entering or amending any insurance policy required hereunder, the Loan Parties shall provide Agent with copies of such policies and shall promptly deliver to Agent updated insurance certificates with respect to such policies.

6.3 Indemnity. Each Loan Party agrees to indemnify and hold Agents, each Lender and their officers, directors, employees, agents, in-house attorneys, representatives and shareholders (each, an "Indemnified Person") harmless from and against any and all claims, costs, expenses, damages and liabilities (including such claims, costs, expenses, damages and liabilities based on liability in tort, including strict liability in tort), including reasonable attorneys' fees and disbursements and other costs of investigation or defense (including those incurred upon any appeal) (collectively, "Liabilities"), that may be instituted or asserted against or incurred by such Indemnified Person as the result of credit having been extended, suspended or terminated under this Agreement and the other Loan Documents or the administration of such credit, or in connection with or arising out of the transactions contemplated hereunder and thereunder, or any actions or failures to act in connection therewith, or arising out of the disposition or utilization of or enforcement of rights in respect of the Collateral, including without limitation any obligations of reimbursement or indemnity under the Account Control Agreements, but excluding in all cases Liabilities to the extent resulting solely from any Indemnified Person's gross negligence or willful misconduct, as determined by a final non-appealable order of a court of competent jurisdiction. In no event shall any Indemnified Person be liable on any theory of liability for any special, indirect, consequential or punitive damages (including any loss of profits, business or anticipated savings). This Section 6.3 shall survive the repayment of indebtedness under, and otherwise shall survive the expiration or other termination of, the Loan Agreement and the resignation or removal of Agent, in each case subject to the applicable statute of limitations. Furthermore, this Section 6.3 shall not apply with respect to Taxes other than any Taxes that represent losses, claims, damages, etc. arising from any non-Tax claim.

SECTION 7. COVENANTS OF THE LOAN PARTIES

Each Loan Party agrees as follows:

7.1 Financial Reports. Borrower shall furnish to the Agent (for delivery to the Lenders) the financial statements and reports listed hereinafter (the "Financial Statements"):

(a) if Borrower's Market Capitalization (measured based on the applicable trading days for the immediately preceding calendar month in a manner otherwise consistent with the definition of "Market Capitalization") is less than $[***] as of [***], as soon as practicable after the end of each month (and in any event within [***] days of such month), unaudited interim and year-to-date financial statements of Borrower as of the end of such month, including balance sheet and related statements of income and cash flows, all certified by Borrower's Chief Executive Officer or Chief Financial Officer to the effect that they have been prepared in accordance with GAAP, (i) except for the absence of footnotes, (ii) subject to normal year-end adjustments, and (iii) except for certain non-cash items that are customarily included in quarterly and annual financial statements;

(b) (i) as soon as practicable (and in any event no later than the earlier of (x) [***] days after the end of such fiscal quarter or for any fiscal quarter with respect to which a later time period as may be provided by the Securities and Exchange Commission pursuant to any releases and extensions thereof in connection with reporting delays caused by COVID-19, such later date provide by the SEC and (y) [***] days after Borrower's Board or an authorized committee thereof has approved such financials) after the end of each calendar quarter, unaudited interim and year-to-date consolidated financial statements of Borrower as of the end of such calendar quarter, including balance sheet and related statements of income and cash flows certified by Borrower's Chief Executive Officer or Chief Financial Officer to the effect that they have been prepared in accordance with GAAP, (A) except for the absence of footnotes, and (B) subject to normal year-end adjustments; and (ii) if Borrower changes its accounting practices to perform a quarterly fair value analysis of its Equity Interests, copies of such valuations when completed, if any; and

(c) as soon as practicable (and in any event no later than the earlier of (x) [***] days after the end of such fiscal year and (y) [***] days after Borrower's Board or an authorized committee thereof has approved such financial statements) after the end of each fiscal year, unqualified audited financial statements of Borrower (other than in respect of a "going concern" qualification, if any), prepared on a consolidated basis, including balance sheet and related statements of income and cash flows, and setting forth in comparative form the corresponding figures for the preceding fiscal year, certified by a firm of independent certified public accountants selected by Borrower and reasonably acceptable to the Required Lenders;

(d) as soon as practicable (and in any event within [***] days) after the end of each fiscal quarter in which financial statements are delivered pursuant to Section 7.1(b), a Compliance Certificate in the form of Exhibit F;

(e) promptly after the filing thereof, copies of any regular, periodic and special reports or registration statements that Borrower files with the Securities and Exchange Commission or any governmental authority that may be substituted therefor, or any national securities exchange;

(f) as soon as practicable (and in any event within [***] days) after the end of each fiscal quarter in which financial statements are delivered pursuant to Section 7.1(b), (x) a cash balance report of the Loan Parties, on a consolidating (or, at the election of Borrower, consolidated) basis, and of the non-Loan Party Platform Companies, on a consolidating (or, at the election of Borrower, consolidated) basis and (y) an accounting of Investments or Dispositions made as of the end of the relevant period in each non-Loan Party Platform Company, Pass-through Entity, other Subsidiary of Borrower or joint venture (whether by capital contribution, transfer or other Disposition of assets, the acquisition of the Equity Interests thereof or in connection with a joint venture, corporate collaboration or similar corporate structure);

(g) financial and business projections and budget promptly following their approval by Borrower's Board or an authorized committee thereof (each, "Board Approved Projections"), and in any event, within [***] days after the end of Borrower's fiscal year and promptly after any material update to such projections or budget is approved by Borrower's Board or an authorized committee thereof, in each case as well as any other budgets, operating plans and other financial information or information with respect to the Collateral or the Platform Companies as may be reasonably requested by Agent or the Required Lenders;

(h) within [***] Business Days of the acquisition of Collateral consisting of Equity Interests or Instruments, notification thereof, together with such originals and other documents as required pursuant to Section 7.18;

(i) within [***] Business Days of (i) the formation of a new Platform Company, (ii) any material amendment, restatement, supplement or other modification of or to any Organizational Document of a Platform Company, and (iii) the entering into of any new material Equity Documents with respect to a Platform Company's Equity Interests, any material amendment, restatement, supplement or other modification of or to any such Equity Document, copies of such Organizational Documents, Equity Documents or applicable amendment, restatement, supplement or modification, as the case may be;

(j) together with the quarterly financial statements, copies of any loan documents entered into by a Platform Company or any Subsidiary thereof with respect to Indebtedness for borrowed money of a Platform Company or such Subsidiary, and any material amendment or other modification thereto, in each case to the extent permitted by law or contract;

(k) promptly after any material amendment, restatement, supplement or other modification to or of any Organizational Document or Equity Document of a Loan Party, a copy thereof;

(l) within [***] Business Days of the occurrence of a Prepayment Event, a notification thereof, together with a description of such Prepayment Event, copies of such documents entered into in connection with the transaction giving rise to the Prepayment Event as Agent may reasonably request and calculations in form reasonably acceptable to Lenders of the amount of Net Cash Proceeds, if any, arising from such Prepayment Event;

(m) promptly upon any legal process in an amount greater than $[***] affecting the Collateral, a notification thereof;

(n) within [***] Business Days of the occurrence of any Default or Event of Default, a notification thereof; ~~and~~

(o) promptly (and in any event within [***] Business Days), notice if any Loan Party or any Subsidiary has knowledge that any Loan Party, or any Subsidiary or Affiliate of any Loan Party, is listed on the OFAC Lists or (a) is convicted of, (b) pleads *nolo contendere* to, (c) is indicted on, or (d) is arraigned and held over on charges involving money laundering or predicate crimes to money laundering~~.~~;

(p) **solely with respect to any Prepayment Event that resulted in any Budgeted Amount being deducted from the applicable Cash proceeds received therefrom, every other fiscal quarter, concurrently with the delivery of quarterly Financial Statements pursuant to Section 7.1(b) for the applicable quarter, and on the last day of the applicable Budgeted Period, a revised budget with respect to the applicable Budgeted Amount in form of presentation reasonably satisfactory to the Required Lenders, certified by the Chief Executive Officer or the Chief Financial Officer of Borrower, which updated budget shall**

include actual expenses paid and projected future expenses, and which shall set forth in comparative form the corresponding figures from the initial budget (or the most recent updated budget delivered pursuant to this clause (p)); and

(q) **solely with respect to any Prepayment Event that resulted in any Budgeted Amount being deducted from the applicable Cash proceeds received therefrom, concurrently with each delivery of quarterly Financial Statements pursuant to Section 7.1(b), a certification by the Chief Executive Officer or the Chief Financial Officer of Borrower that any portion of any Budgeted Amount withdrawn from a Controlled Account during the period covered by such Financial Statements was used solely for expenses directly attributable to the performance of obligations by any Platform Company or associated Loan Party in connection with the applicable Prepayment Event.**

Notwithstanding the foregoing, documents required to be delivered under this Section 7 may be delivered electronically and shall be deemed delivered when Borrower posts a link to such publicly disclosed documents on its publicly available website.

No Loan Party shall make any change in its (a) accounting policies or reporting practices other than to the extent required or otherwise contemplated by GAAP or other applicable regulatory requirements, or (b) fiscal years or fiscal quarters. The fiscal year of Borrower shall end on December 31.

Each executed Compliance Certificate may be sent via email to Administrative Agent at [***]; [***]; [***]. All Financial Statements required to be delivered pursuant to clauses (a), (b) and (c) shall be sent via e-mail to [***] with a copy to [***]; [***] with a copy to [***]; and, provided, that if e-mail is not available or sending such Financial Statements via e-mail is not possible, they shall be faxed to Administrative Agent at: [***], attention: [***].

7.2 Inspection Rights. The Borrower shall permit any representative that Agent or the Required Lenders authorize in writing, including its attorneys and accountants, to inspect the Collateral and examine and make copies and abstracts of the books of account and records of Borrower (and, if requested by such representative of Agent or the Required Lenders, consolidating financial statements of Borrower, each Loan Party and each Platform Company for any relevant period or periods as may be reasonably so requested) at reasonable times and upon reasonable notice during normal business hours; provided, however, that so long as no Event of Default has occurred and is continuing, such examinations and request for consolidating financial statements shall be limited to no more often than [***] per fiscal year. In addition, any such representative shall have the right to meet with management and officers of Borrower to discuss such books of account and records at reasonable times and upon reasonable written notice. In addition, Agent or any Lender shall be entitled at reasonable times and intervals to consult with and advise the management and officers of Borrower concerning significant business issues affecting Borrower, the Loan Parties and their businesses and Subsidiaries. Such consultations shall not unreasonably interfere with Borrower's business operations. The parties intend that the rights under this paragraph shall permit Agent or Lenders solely the right to information and consultation and not be deemed to give Agent or any Lender any right to exercise control or any rights of operations with respect to Borrower or its business or operations.

7.3 Further Assurances. Each Loan Party shall from time to time execute, deliver and file, alone or with the Collateral Agent (but without obligation to do so), any financing statements, security agreements, collateral assignments, notices, control agreements, or other documents to perfect or give the highest priority to the Collateral Agent's Lien on the Collateral.

Each Loan Party shall from time to time procure any instruments or documents, and take all further action that may be necessary, or that the Collateral Agent may reasonably request (as directed by the Required Lenders) in writing, to perfect and protect the Liens granted hereby and thereby. In addition, and for such purposes only, each Loan Party hereby authorizes the Collateral Agent (but without obligation) to execute and deliver on behalf of such Loan Party and to file such financing statements (including an indication that the financing statement covers "all assets or all personal property" of such Loan Party in accordance with Section 9-504 of the UCC), and each Loan Party hereby authorizes the Collateral Agent, at any time during the existence of an Event of Default, to execute and deliver on behalf of such Loan Party any collateral assignments, notices, control agreements, security agreements and other documents without the signature of such Loan Party either in the Collateral Agent's name or in the name of the Collateral Agent as agent and attorney-in-fact for such Loan Party if such Loan Party does not deliver the same within [***] Business Days of the Collateral Agent's request. Each Loan Party shall protect and defend such Loan Party's title to the Collateral and the Collateral Agent's Lien thereon against all Persons claiming any interest adverse to such Loan Party or Agent other than Permitted Liens. Notwithstanding the foregoing or anything to the contrary herein or in any other Loan Document, the Collateral Agent shall not be responsible for the preparation, filing, form, content or continuation of any UCC financing statements, mortgages, intellectual property security agreements, assignments, conveyances, financing statements, transfer endorsements or similar instruments. For the avoidance of doubt, the Required Lenders (or counsel to the Required Lenders) shall make all filings (including filings of continuation statements and amendments to UCC financing statements that may be necessary to continue the effectiveness of such UCC financing statements) necessary to maintain (at the sole cost and expense of the Borrower) the security interest created by the Loan Documents in the Collateral as a first priority perfected security interest to the extent perfection is required herein or by the Loan Documents, and promptly provide evidence thereof to the Collateral Agent.

7.4 Indebtedness. No Loan Party shall create, incur, assume, guarantee or be or remain liable with respect to any Indebtedness, other than Permitted Indebtedness, or prepay, redeem or cash settle any Indebtedness or take any actions which impose on any Loan Party an obligation to prepay, redeem or cash settle any Indebtedness, except for (a) the conversion of Indebtedness into equity securities and the payment of Cash in lieu of fractional shares in connection with such conversion, (b) with respect to purchase money Indebtedness permitted hereunder to the extent the outright purchase of such equipment would constitute an Investment in a capital asset that is permitted, (c) the foregoing to the extent refinanced with similar Permitted Indebtedness (provided that (w) the principal amount of such Indebtedness being refinanced is not increased, (x) the Indebtedness as so refinanced does not shorten the maturity or weighted average life to maturity of the Indebtedness being refinanced, (y) if the Indebtedness being refinanced is Subordinated Indebtedness, the Indebtedness as so refinanced is Subordinated Indebtedness and (z) if the Indebtedness being refinanced is Permitted Convertible Indebtedness, such refinancing (whether in the form of a redemption or otherwise) is consummated in compliance with the immediately following paragraph; or (d) as otherwise permitted hereunder or approved in writing by the Required Lenders or Agent, as directed by the Required Lenders.

Notwithstanding anything to the contrary in the foregoing, the issuance of, performance of obligations under (including any payments of interest), and conversion, exercise, repurchase, redemption (including, for the avoidance of doubt, a redemption of Permitted Convertible Debt upon satisfaction of a condition, if any, related to the stock price of Borrower's common stock set forth in the indenture (or other agreement) governing the Permitted Convertible Debt), settlement or early termination or cancellation of (whether in whole or in part and including by netting or set-off) (in each case, whether in Cash, common stock of Borrower, Permitted Convertible Debt or, following a merger event or other change of the common stock of Borrower, other securities or property), or the satisfaction of any condition that would permit or require any of the foregoing, any Permitted Convertible Debt shall not constitute a prepayment of Indebtedness by Borrower for the purposes of this Section 7.4; provided that Borrower shall not be permitted to redeem or repurchase, (in part or in full) Permitted Convertible Debt with cash consideration (including via open-market repurchases with cash consideration) unless, after giving pro forma effect to such redemption or repurchase of such Permitted Convertible Debt: (a) no Default or Event of Default shall exist or would result therefrom and (b) the Loan Parties' Qualified Cash shall be equal to or greater than [***]% of the outstanding Secured Obligations.

Notwithstanding anything to the contrary herein, no Loan Party shall permit or suffer Platform Companies which are not Loan Parties to (x) create, incur, assume, guarantee or be or remain liable with respect to any Indebtedness (other than intercompany Indebtedness constituting Permitted Investments or other Permitted Indebtedness of the types described in clauses (c) (to the extent not [***] days or more past the invoice date), (e), (h), (i), (p), (q), (r) (to the extent not in an outstanding amount in excess of, when combined with the amount incurred by Loan Parties under such clause (r) at such time, the maximum aggregate amount specified in such clause) or (s) of the definition of "Permitted Indebtedness") in excess of $[***] in the aggregate at any one time outstanding for all such Platform Companies or (y) consummate any royalty financings or similar transactions other than Permitted Royalty Transactions.

No Loan Party shall guarantee or be or remain liable with respect to any Indebtedness of BB Square Capital.

7.5 Liens. Each Loan Party shall at all times keep the Collateral and all other property and assets used in the Loan Parties' business or in which the Loan Parties now or hereafter holds any interest free and clear from any Liens whatsoever (except for Permitted Liens). No Loan Party shall agree with any Person other than Agent or Lenders not to encumber the Collateral, other than pursuant to Permitted Indebtedness incurred pursuant to clauses (b), (e), (f), (h), (t), (t), (u) and (w) of the definition thereof and except for restrictions on the granting of Liens (other than Permitted Liens and the Liens pursuant to the Loan Documents) in any Loan Party's Organizational Documents not otherwise restricted hereunder.

Notwithstanding anything to the contrary herein, no Loan Party shall permit or suffer Platform Companies which are not Loan Parties to (x) create, incur, assume, guarantee or be or remain liable with respect to, or suffer to exist, any Indebtedness that is secured by Liens in excess of $[***] in the aggregate at any one time outstanding for all such Platform Companies or (y) consummate any royalty financings or similar transactions other than Permitted Royalty Transactions which are secured by Liens of the type described in clause (s) of the definition of "Permitted Liens".

7.6 Investments. No Loan Party shall, directly or indirectly acquire or own, or make any Investment in or to any Person other than Permitted Investments.

Notwithstanding the foregoing, and for the avoidance of doubt, this Section 7.6 shall not prohibit the conversion by holders of (including any payment upon conversion, whether in Cash, common stock or a combination thereof), or required payment of any principal or premium on (including, for the avoidance of doubt, in respect of a redemption of Permitted Convertible Debt upon satisfaction of a condition, if any, related to the stock price of Borrower's common stock set forth in the indenture (or other agreement) governing the Permitted Convertible Debt) or required payment of any interest with respect to, any Permitted Convertible Debt in each case, in accordance with the terms of the indenture (or other agreement) governing such Permitted Convertible Debt, subject in each case, to the extent applicable pursuant to the second paragraph of Section 7.4, to compliance therewith.

Notwithstanding the foregoing, Borrower may repurchase, exchange or induce the conversion of Permitted Convertible Debt by delivery of shares of Borrower's common stock and/or a different series of Permitted Convertible Debt, or by payment of Cash in an amount that does not exceed the net cash proceeds received by Borrower from a substantially concurrent issuance of shares of Borrower's common stock and/or Permitted Convertible Debt plus the net cash proceeds, if any, received by Borrower pursuant to the related exercise or early unwind or termination of the related Permitted Bond Hedge Transactions and Permitted Warrant Transactions, if any, pursuant to the immediately following proviso; provided that, for the avoidance of doubt, Borrower may exercise or unwind or terminate early (whether in Cash, shares or any combination thereof) the portion of the Permitted Bond Hedge Transactions and Permitted Warrant Transactions, if any, corresponding to such Permitted Convertible Debt that are so repurchased, exchanged or converted.

Notwithstanding the foregoing, Borrower may repurchase its common stock with up to an amount equal to [***]% of (x) the net cash proceeds from a substantially concurrent issuance and sale of Permitted Convertible Debt, less (y) the proceeds from such issuance and sale of Permitted Convertible Debt which are used to redeem, cash settle, prepay, exchange, convert or otherwise refinance any existing Permitted Convertible Debt (including related interest, fees, expenses and premiums payable in respect thereof).

Notwithstanding anything to the contrary herein, no Loan Party shall legally or beneficially transfer the title of, or otherwise Dispose of, or make an Investment consisting of, or otherwise transfer or distribute, any of its Material Intellectual Property (or the exclusive rights thereto) to a Platform Company, Subsidiary or Affiliate that is not a Loan Party.

Notwithstanding the foregoing, (x) from and after the Closing Date and until the occurrence of the Milestone Satisfaction Date, no Loan Party may make any additional Investments in [***] and (y) from and after the occurrence of the Milestone Satisfaction Date, Loan Parties may make additional Investments in [***], provided that the aggregate additional Investments made by the Loan Parties in [***] shall not exceed (a) $[***] in the aggregate, plus (b) up to $[***] in additional Investment made by the Loan Parties in [***] in any fiscal year for operating, overhead or other expenses; provided in each case that Borrower and/or one or more other Loan Parties or Pass-through Entities shall pledge the Equity Interests which Borrower and/or any other Loan Party or Pass-through Entity holds in [***] as Pledged Collateral (each such Investment, a "[***]"). For the avoidance of doubt, any Investments made in [***] prior to the Closing Date shall not reduce the available amounts under clauses (a) and (b) above and such previously made Investments may remain invested in [***].

7.7 Distributions. No Loan Party shall (a) repurchase or redeem any class of stock or other Equity Interest of any Loan Party or the Equity Interests of any of its Subsidiaries other than repurchases described in clauses (c), (k), (t) and (u) of the defined term "Permitted Investments"; (b) declare or pay any cash dividend or make a cash distribution on any class of stock or other Equity Interest, except for (i) distributions of Net Cash Proceeds, to the extent any Lenders shall have waived the application of any portion of such Net Cash Proceeds to the mandatory prepayment and to the extent the Required Lenders have consented to the distribution in respect of any portion of such Net Cash Proceeds to a Loan Party's members, (ii) any distributions made by a Loan Party to another Loan Party (provided that in the case of any such distribution by any

Loan Party that is not directly or indirectly a wholly-owned Subsidiary of Borrower, such distribution is made to Borrower or another Loan Party on no less than Borrower or such Loan Party's relative ownership interests of the relevant Equity Interests of such non-wholly owned Loan Party), or (iii) subject to satisfaction of the Equity Cash Payment Conditions, any payments made by a Loan Party related to a tender offer as permitted in accordance with any equity exchange program involving the issuance of equity awards under a Loan Party's equity incentive plans; (c) lend money to any employees, officers, managers or directors or guarantee the payment of any such loans granted by a third party in excess of $[***] in any fiscal year; or (d) waive, release or forgive any Indebtedness owed by any employees, officers, managers or directors in excess of $[***] in any fiscal year. Notwithstanding anything to the contrary herein, the Loan Parties may issue additional Equity Interests and make payments to employees of the Borrower or its Subsidiaries in connection with the exercise or vesting of stock options, stock appreciation rights, restricted stock units, restricted stock or similar equity incentives or equity-based incentive plan in the ordinary course of business and consistent with past practice.

Notwithstanding the foregoing, and for the avoidance of doubt, this Section 7.7 shall not prohibit (i) the conversion by holders of (including any Cash payment upon conversion), or required payment of any principal or premium on (including, for the avoidance of doubt, in respect of a redemption of Permitted Convertible Debt upon satisfaction of a condition, if any, related to the stock price of Borrower's common stock set forth in the indenture (or other agreement) governing the Permitted Convertible Debt) or required payment of any interest with respect to, any Permitted Convertible Debt in each case, in accordance with the terms of the indenture (or other agreement) governing such Permitted Convertible Debt, or (ii) the entry into (including the payment of premiums in connection therewith) or any required payment with respect to, or required early unwind or settlement of, any Permitted Bond Hedge Transaction or Permitted Warrant Transaction, in each case, in accordance with the terms of the agreement governing such Permitted Bond Hedge Transaction or Permitted Warrant Transaction, subject in each case of the foregoing clauses (i) and (ii), to the extent applicable pursuant to the second paragraph of Section 7.4, to compliance therewith.

Notwithstanding the foregoing, Borrower may repurchase, exchange or induce the conversion of Permitted Convertible Debt by delivery of shares of Borrower's common stock and/or a different series of Permitted Convertible Debt and/or by payment of Cash in an amount that does not exceed the net cash proceeds received by Borrower from the substantially concurrent issuance of shares of Borrower's common stock and/or Permitted Convertible Debt plus the net cash proceeds, if any, received by any Loan Party pursuant to the related exercise or early unwind or termination of the related Permitted Bond Hedge Transactions and Permitted Warrant Transactions, if any, pursuant to the immediately following proviso; provided that, for the avoidance of doubt, Borrower may exercise or unwind or terminate early (whether in Cash, shares or any combination thereof) the portion of the Permitted Bond Hedge Transactions and Permitted Warrant Transactions, if any, corresponding to such Permitted Convertible Debt that are so repurchased, exchanged or converted.

Notwithstanding the foregoing, Borrower may repurchase its common stock with up to an amount equal to [***]% of (x) the net cash proceeds from a substantially concurrent issuance and sale of Permitted Convertible Debt, less (y) the proceeds from such issuance and sale of Permitted Convertible Debt which are used to redeem, cash settle, prepay, exchange, convert or otherwise refinance any existing Permitted Convertible Debt (including related interest, fees, expenses and premiums payable in respect thereof).

Notwithstanding anything to the contrary herein, no Loan Party shall legally or beneficially transfer the title of, or otherwise Dispose of, or make an Investment consisting of, or otherwise transfer or distribute, any of its Material Intellectual Property (or the exclusive rights thereto) to a Platform Company, Subsidiary or Affiliate that is not a Loan Party.

7.8 Transfers. Except for Permitted Transfers, no Loan Party shall voluntarily or involuntarily make any Dispositions.

Notwithstanding anything to the contrary herein, no Loan Party shall legally or beneficially transfer the title of, or otherwise Dispose of, or make an Investment consisting of, or otherwise transfer or distribute, any of its Material Intellectual Property (or the exclusive rights thereto) to a Platform Company, Subsidiary or Affiliate that is not a Loan Party.

Notwithstanding anything herein to the contrary, to the extent any Platform Company, Pass-through Entity, other Subsidiary of the Borrower or any joint venture is required to become a Guarantor pursuant to Section 7.13, then no further Dispositions, transfers, distributions or Investments may be made in such Platform Company, Pass-through Entity, other Subsidiary of the Borrower or any joint venture until such Platform Company, Pass-through Entity, other Subsidiary of the Borrower or any joint venture has become a Guarantor in accordance with this Agreement.

Except for a [***], no Loan Party shall Dispose of or otherwise transfer, distribute or Invest any of its assets to or in [***].

7.9 Mergers or Acquisitions. No Loan Party shall merge or consolidate with or into any other Person, except that (i) any Subsidiary of a Loan Party may merge with, consolidate with or into, dissolve or liquidated into a Loan Party, provided that such Loan Party shall be the continuing or surviving entity and all actions reasonably required by Agent (as directed by the Required Lenders), including actions required to maintain perfected Liens on the Equity Interests of the surviving entity and other Pledged Collateral in favor of Agent shall have been completed in accordance with the terms of this Agreement, (ii) any Loan Party may merge with, consolidate with or into, dissolve or liquidated into another Loan Party, provided that if such transaction involves Borrower, then Borrower must be the continuing or surviving entity, (iii) any Loan Party may effect the formation, dissolution, liquidation or Disposition of any Subsidiary that is a Delaware Divided LLC, provided that Borrower is in compliance with Section 7.13 or (iv) any Loan Party may make Acquisitions or other Investments in compliance with Section 7.6 and otherwise permitted hereunder (including Section 7.13).

7.10 Taxes. Each Loan Party shall pay when due all material Taxes, fees or other charges of any nature whatsoever (together with any related interest or penalties) now or hereafter imposed or assessed against such Loan Party or the Collateral or upon such Loan Party's ownership, possession, use, operation or disposition thereof or upon such Loan Party's rents, receipts or earnings arising therefrom, unless the same are being contested in good faith and by appropriate proceedings and adequate reserves in accordance with GAAP are being maintained by such Loan Party. Each Loan Party shall file on or before the due date therefor all material personal property Tax returns in respect of the Collateral.

7.11 Certain Changes. No Loan Party shall:

(a) permit or suffer a Change in Control to occur;

(b) change its jurisdiction of organization, organizational form or legal name without [***] days' prior written notice to Agent; or

(c) amend, restate, supplement or otherwise modify the terms of the Organizational Documents of any Loan Party if the effect of such change could be expected to be materially adverse to the interests of Agent or the Lenders.

7.12 Deposit Accounts. No Loan Party shall maintain any Deposit Accounts, or accounts holding Investment Property, except for Excluded Accounts and accounts with respect to which Collateral Agent has an Account Control Agreement, provided, that the Loan Parties shall have [***] days following the establishment or acquisition of any new Deposit Account or account holding Investment Property (other than Excluded Accounts) to enter into and cause each applicable depository or securities intermediary to enter into, an Account Control Agreement.

7.13 Platform Companies; Additional Guarantors.

(a) No Loan Party shall permit the Organizational Documents of any Platform Company, or any of its Equity Documents to contain any provision, unless waived, which would restrict, delay or condition the grant of the security interest in the Pledged Collateral as set forth in this Agreement or the exercise of any remedy with respect to the Pledged Collateral, including, without limitation, the exercise of voting rights by Agent or the disposition of the Pledged Collateral after the occurrence and during the continuation of an Event of Default.

(b) Borrower shall, within [***] days of (i) any Platform Company initiating a Phase 3 Study or acquiring rights or an exclusive License to any product that is the subject of an existing Phase 3 Study or (ii) formation, dissolution, liquidation or Disposition of any Subsidiary that is a Delaware Divided LLC, in each case of the foregoing clauses (i) and (ii), cause such Platform Company or Subsidiary to execute and deliver to Agent a Joinder Agreement.

(c) Borrower shall, within [***] days of (x) Borrower and/or the other Loan Parties having made (whether prior to, on or after the Closing Date), in the aggregate, more than $[***] of Investments or Dispositions at any time in any single Platform Company, Pass-through Entity, any other Subsidiary of Borrower or joint venture (whether by capital contribution, transfer or other Disposition of assets, the acquisition of the Equity Interests thereof or in connection with a joint venture, corporate collaboration or similar corporate structure), other than BB Square Capital, cause such Platform Company, Pass-through Entity, Subsidiary or joint venture to execute and deliver to Agent a Joinder Agreement and become a Guarantor hereunder or (y) the formation or establishment of any Pass-through Entity which directly or indirectly holds any Equity Interests in any Platform Company (other than the Pass-through Entity BridgeBio Pharma Cayman), cause such Pass-through Entity to execute and deliver to Agent a Joinder Agreement and become a Guarantor hereunder; provided that, notwithstanding anything herein to the contrary, (i) on or prior to [***], Borrower shall only be required to cause [***] or [***] to become a Guarantor hereunder if the aggregate amount of Investments or Dispositions made by Borrower and/or the other Loan Parties in each such Person exceeds $[***], and after [***], Borrower shall only be required to cause either such Person to become a Guarantor hereunder if the aggregate amount of Investments or Dispositions made by Borrower and/or the other Loan Parties in each such Person exceeds $[***] and (ii) at all times, Borrower shall only be required to cause [***] to become a Guarantor hereunder if the aggregate amount of Investments or Dispositions made by Borrower and/or the other Loan Parties in such Person exceeds $[***]. If two or more Platform Companies, Pass-through Entities, Subsidiaries or joint ventures merge or consolidate with one another or enter into any arrangement in which such Platform Companies, Pass-through Entities, Subsidiaries or joint ventures have access to or share any assets or property (including any licensing arrangement), the amount of Investments or Dispositions by Borrower and/or the other Loan Parties with respect to each Platform Company, Pass-through Entity, Subsidiary or joint venture will be calculated on a consolidated basis based on Investments by or Dispositions from the Loan Parties in each such Platform Company, Pass-through Entity, Subsidiary or joint venture prior to such merger, consolidation or similar transaction and any additional Investments or Dispositions made by the Loan Parties in connection with or subsequent to such Investment, Disposition, merger, consolidation or similar transaction. In addition, the amount of Investments or Dispositions shall include any amount of Investments and Dispositions initially made by a Loan Party in one Platform Company, Pass-through Entity, Subsidiary or joint venture and subsequently transferred or invested in another Platform Company, Pass-through Entity, Subsidiary or joint venture.

7.14 Use of Proceeds. Borrower agrees that the proceeds of the Loans shall be used solely to fund the Refinancing and pay related fees and expenses in connection therewith (in the case of the Tranche I Advance) and to pay related fees and expenses in connection with this Agreement and for working capital and general business purposes, including, without limitation, Investments in Platform Companies, the Loan Parties' clinical development and commercial efforts, and repurchases of common stock of Borrower or repurchases or redemptions of Permitted Convertible Debt, in each case to the extent permitted hereunder. The proceeds of the Loans will not be used in violation of Anti-Corruption Laws or applicable Sanctions.

7.15 Compliance with Laws.

(a) Each Loan Party shall maintain compliance in all material respects with all applicable laws, rules or regulations, and shall, or shall cause its Subsidiaries to, obtain and maintain all required governmental authorizations, approvals, licenses, franchises, permits or registrations reasonably necessary in connection with the conduct of such Loan Party's business; and no Loan Party shall become an "investment company" or a company controlled by an "investment company", under the Investment Company Act.

(b) No Loan Party shall, nor shall a Loan Party permit any controlled Affiliate to, directly or indirectly, knowingly enter into any documents, instruments, agreements or contracts with any Person listed on the OFAC Lists. No Loan Party shall (i) conduct any business or engage in any transaction or dealing with any Blocked Person, including, without limitation, the making or receiving of any contribution of funds, goods or services to or for the benefit of any Blocked Person, (ii) deal in, or otherwise engage in any transaction relating to, any property or interests in property blocked pursuant to Executive Order No. 13224 or any similar executive order or other Anti-Terrorism Law, or (iii) engage in or conspire to engage in any transaction that evades or avoids, or has the purpose of evading or avoiding, or attempts to violate, any of the prohibitions set forth in Executive Order No. 13224 or other Anti-Terrorism Law, nor shall a Loan Party knowingly permit any controlled Affiliate to, directly or indirectly do any of the foregoing.

(c) Each Loan Party has implemented and maintains in effect policies and procedures designed to ensure compliance by such Loan Party, and its respective directors, officers, managers, employees, and agents with Anti-Corruption Laws and applicable Sanctions, and each Loan Party, and its respective officers and employees and, to the knowledge of such Loan Party, its directors, managers and agents, are in compliance with Anti-Corruption Laws and applicable Sanctions in all material respects.

(d) No Loan Party, or any of its respective directors, officers, managers or employees, or to the knowledge of such Loan Party, any agent for such Loan Party that will act in any capacity in connection with or benefit from the credit facility established hereby, is a Sanctioned Person. No Loan, use of proceeds or other transaction contemplated by this Agreement will violate Anti-Corruption Laws or applicable Sanctions.

7.16 Intellectual Property. Each Loan Party shall (i) protect, defend and maintain the validity and enforceability of its Intellectual Property necessary for its continued operations; (ii) promptly advise Agent in writing of material infringements of its Material Intellectual Property; and each Loan Party shall use reasonable efforts to prevent any Intellectual Property material to such Loan Party's business from being abandoned, forfeited or dedicated to the public. If any Loan Party (i) obtains any Patent, registered Trademark, registered Copyright, registered mask work, or any pending application for any of the foregoing, whether as owner, licensee or otherwise, or (ii) applies for any Patent or the registration of any Trademark, Copyright or mask work then such Loan Party shall on the next Compliance Certificate required to be delivered hereunder provide written notice thereof to Agent and shall execute such intellectual property security agreements and other documents and take such other actions as necessary or as Agent (as directed by the Required Lenders) may request in its good faith business judgment to perfect and maintain a first priority perfected security interest in favor of Agent in such property. The Loan Parties shall, together with the delivery of the next Compliance Certificate required to be delivered hereunder, provide to Agent copies of all applications that it files for Patents or for the registration of Trademarks, Copyrights or mask works, together with evidence of the recording of the intellectual property security agreement required for Agent to perfect and maintain a first priority perfected security interest in such property.

7.17 Transactions with Affiliates. No Loan Party shall, directly or indirectly, enter into or permit to exist any transaction of any kind with any Affiliate of any Loan Party on terms that are less favorable to the Loan Parties, other than those that might be obtained in an arm's length transaction from a Person who is not an Affiliate of a Loan Party, except that no Loan Party shall be subject to the foregoing limitation with respect to (i) issuance of Subordinated Indebtedness or Equity Interests, including to existing investors, (ii) entrance into customary compensation arrangements in the ordinary course of business and approved by the Board or an authorized committee thereof, (iii) consummation of any Permitted Transfer expressly contemplated to be entered into between a Loan Party and an Affiliate, or (iv) any distribution permitted pursuant to Section 7.7.

7.18 Pledged Collateral. Any Loan Party shall (a) at such Loan Party's expense, promptly execute, acknowledge and deliver all such instruments and take all such actions as Agent or the Required Lenders from time to time may reasonably request in order to ensure to Agent the benefits of the pledge intended to be created by Section 3.3, shall maintain, preserve and defend the title to the Pledged Collateral and the Lien of Agent thereon against the claim of any other Person (other than Permitted Liens); and (b) upon acquiring any new Equity Interests constituting Pledged Collateral or Instruments constituting Collateral, within [***] Business Days (i) deliver to Agent an updated Schedule 5.15 hereto, in form reasonably satisfactory to Agent, identifying such additional Equity Interests, which shall be attached to this Agreement, (ii) either deliver or otherwise cause the transfer of such additional Equity Interests or Instruments (including any certificates and duly executed transfer powers or other instruments of transfer executed in blank and in form and substance satisfactory to the Required Lenders) to Agent as required under this Agreement or any Loan Document or enter into a control agreement in favor of Agent in form acceptable to the Required Lenders and to Agent as to its rights, duties and obligations with respect thereto, provided that with respect to Equity Interests of any Loan Party other than Borrower, to the extent the Organizational Documents of such Loan Party do not provide for the issuance of physical stock certificates and as long as no physical stock certificates are issued, such Loan Party shall not be required to deliver stock certificates, stock powers or control agreements, and (iii) to the extent related to an Investment in a new Platform Company, deliver an acknowledgement, consent and waiver in substantially the form delivered by the Platform Companies as of the Closing Date. No Loan Party shall enter into any agreement restricting its ability to vote the Equity Interests or assigning or otherwise transferring or restricting its ability to vote the Equity Interests owned by such Loan Party other than pursuant to any Loan Document or in connection with voting agreements entered into by holders of Equity Interests in each Platform Company on customary terms for venture capital financings, in each case, which are not designed to impair the pledge or Collateral Agent's exercise of remedies with respect to Pledged Collateral.

7.19 Post-Closing Deliveries. The applicable Loan Parties shall deliver the documents or take the actions as set forth in Schedule 7.19 hereto with the time period(s) set forth therein (or such longer periods as the Required Lenders may agree in their discretion).

7.20 [Reserved.]

7.21 [Reserved.]

7.22 Foreign Subsidiary or Foreign Subsidiary Holdco. The Loan Parties shall not, and shall not permit any Subsidiary, to amend or modify any governing document of any Foreign Subsidiary or Foreign Subsidiary Holdco, the effect of which is to require a vote of greater than 50.1% of the Equity Interests or voting rights of such entity for any decision or action of such entity.

SECTION 8.[RESERVED]

SECTION 9.EVENTS OF DEFAULT

The occurrence of any one or more of the following events shall be an Event of Default:

9.1 Payments. Any Loan Party fails to pay principal, interest and regularly scheduled fee when due under this Agreement or any other Loan Document, or shall pay any other amount due hereunder within [***] Business Days of the due date; provided, however, that an Event of Default shall not occur on account of a failure to pay due solely to an administrative or operational error of Agent or Lenders or any Loan Party's bank if such Loan Party had the funds to make the payment when due and makes the payment within [***] Business Days following such Loan Party's knowledge of such failure to pay; or

9.2 Covenants. Any Loan Party breaches or defaults in the performance of any covenant or Secured Obligation under this Agreement, or any of the other Loan Documents or any other agreement among any Loan Party, Agent and Lenders, and (a) with respect to a Default under any covenant under this Agreement other than the Sections specifically identified in clause (b) hereof, any other Loan Document or any other agreement between any Loan Party and Agent or Lenders, and such Default continues for more than [***] days, or (b) with respect to a default under any of Sections 6, 7.1, 7.4, 7.5, 7.6, 7.7, 7.8, 7.9, 7.10, 7.11, 7.12, 7.13, 7.14, 7.15, 7.17, 7.18, 7.19, or 7.22 the occurrence of such Default; or

9.3 Change in Control or Material Adverse Effect. A Change in Control occurs, or an event or circumstance that would reasonably be expected to have a Material Adverse Effect has occurred; provided that, failure to achieve the [***] Milestone Date, achieve any Other Milestone or initiate or perform any Phase 3 Study shall not in itself constitute a Material Adverse Effect; or

9.4 Representations. Any representation or warranty made or deemed made by any Loan Party in any Loan Document shall have been false or misleading in any material respect (or, to the extent any such representation or warranty is qualified by any applicable standard of materiality, in all respects) when made or when deemed made; or

9.5 Insolvency. Any Loan Party (i) (A) shall make an assignment for the benefit of creditors; or (B) shall be unable to pay its debts as they become due, or shall become insolvent; or (C) shall file a voluntary petition in bankruptcy; or (D) shall file any petition, answer, or document seeking for itself any reorganization, arrangement, composition, readjustment, liquidation, dissolution or similar relief under any present or future statute, law or regulation pertinent to such circumstances; or (E) shall seek or consent to or acquiesce in the appointment of any trustee, receiver, or liquidator of such Person or of all or any part of the assets or property of such Person; or (F) except as otherwise permitted hereunder, shall cease operations of its business as its business has normally been conducted, or terminate substantially all of its employees; or (G) the Board or majority of the holders of the Equity Interests of the foregoing shall take any action initiating any of the foregoing actions described in clauses (A) through (F); or (ii) either (A) [***] days shall have expired after the commencement of an involuntary action against any Loan Party seeking reorganization, arrangement, composition, readjustment, liquidation, dissolution or similar relief under any present or future statute, law or regulation, without such action being dismissed or all orders or proceedings thereunder affecting the operations or the business of any Loan Party, being stayed; or (B) a stay of any such order or proceedings shall thereafter be set aside and the action setting it aside shall not be appealed within [***] days; or (C) any Loan Party, shall file any answer admitting or not contesting the material allegations of a petition filed against such Loan Party in any such proceedings; or (D) the court in which such proceedings are pending shall enter a decree or order granting the relief sought in any such proceedings; or (E) [***] days shall have expired after the appointment, without the consent or acquiescence of the applicable Loan Party, of any trustee, receiver or liquidator of such Person or of all or any material part of the properties of such Person without such appointment being vacated; or

9.6 Attachments; Judgments. Any material portion of the assets of the Loan Parties, taken as a whole, is attached or seized, or a levy is filed against any such assets, or a final judgment or judgments is/are entered (in each case to the extent not paid and not covered by independent third party insurance, which coverage has been acknowledged by the insurer) for the payment of money individually or in the aggregate, of at least $[***] by any Loan Party, and there is a period of [***] consecutive days during which a stay of enforcement of such judgment, by reason of a pending appeal, bond or otherwise, is not in effect, or any Loan Party is enjoined or in any way prevented by court order from conducting any material part its business; or

9.7 Other Obligations. The occurrence of any Default under any agreement or obligation of any Loan Party or any of its Subsidiaries involving any Indebtedness in excess of $[***], which could entitle or permit any Person to accelerate such Indebtedness or any early cash payment in excess of $[***] by Borrower or its Affiliate is required, or unwinding or termination occurs with respect to either any Permitted Bond Hedge Transaction or any Permitted Warrant Transaction that requires Borrower or its Affiliate to make net cash payments in excess of $[***] in the aggregate, or any condition giving rise to the foregoing is met, in each case, with respect to which Borrower or its Affiliate is the "defaulting party" under the terms of such Permitted Bond Hedge Transaction or Permitted Warrant Transaction.

9.8 Specified Event of Default. The Loan Parties do not have Qualified Cash equal to or greater than [***]% of the outstanding Secured Obligations within [***] days of each time that Borrower settles (in part or in full) Permitted Convertible Debt (other than any scheduled payments, cash settlement payments of less than $[***]in the aggregate in any [***] consecutive day period, or ordinary course fees and expenses thereunder) with cash consideration (including via cash settlement), in each case after giving effect to such settlement.

SECTION 10.REMEDIES

10.1 General. Upon and during the continuance of any one or more Events of Default, Agent may, and at the direction of the Required Lenders shall, (i) accelerate and demand payment of all or any part of the Secured Obligations together with a Prepayment Charge and declare them to be immediately due and payable (provided, that upon the occurrence of an Event of Default of the type described in Section 9.5, all of the Secured Obligations shall automatically be accelerated and made due and payable, in each case without any further notice or act), (ii) sign and file in any Loan Party's name, any and all collateral assignments, notices, control agreements, security agreements and other documents it deems necessary or appropriate to perfect or protect the repayment of the Secured Obligations, and in furtherance thereof, each Loan Party hereby grants Agent an irrevocable power of attorney coupled with an interest, and (iii) notify any of any Loan Party's account debtors to make payment directly to Agent, compromise the amount of any such account on such Loan Party's behalf and endorse Agent's name without recourse on any such payment for deposit directly to Agent's account. Agent may, and at the direction of the Required Lenders shall, exercise all rights and remedies with respect to the Collateral under the Loan Documents or otherwise available to it under the UCC and other applicable law, including the right to release, hold, sell, lease, liquidate, collect, realize upon, or otherwise dispose of all or any part of the Collateral and the right to occupy, utilize, process and commingle the Collateral. All Agent's rights and remedies shall be cumulative and not exclusive.

10.2 Collection; Foreclosure. Upon the occurrence and during the continuance of any Event of Default, Agent shall at the direction of the Required Lenders, at any time or from time to time, apply, collect, liquidate, sell in one or more sales, lease or otherwise Dispose of, any or all of the Collateral, in its then condition or following any commercially reasonable preparation or processing, in such order as Agent may elect. Any such sale may be made either at public or private sale at its place of business or elsewhere. Each Loan Party agrees that any such public or private sale may occur upon [***] calendar days' prior written notice to such Loan Party. Agent may, and at the direction of the Required Lenders shall, require any Loan Party to assemble the Collateral and make it available to Agent at a place designated by Agent. The proceeds of any sale, Disposition or other realization upon all or any part of the Collateral shall be applied by Agent in the following order of priorities:

First, to Agents in an amount sufficient to pay in full the Agents' fees, costs, indemnities, liabilities and related obligations, including reasonable costs and professionals' and advisors' fees and expenses as described in Section 11.11;

Second, to Lenders in an amount sufficient to pay in full the Lenders' fees, costs, indemnities, liabilities and related obligations, including reasonable costs and professionals' and advisors' fees and expenses as described in Section 11.11, ratably among them in proportion to the amounts described in this clause Second payable to them;

Third, to Lenders in an amount equal to the accrued and unpaid interest on the Loans, ratably among the Lenders in proportion to the respective amounts described in this clause Third held by them;

Fourth, to Lenders in an amount equal to the unpaid principal of the Loans, ratably among the Lenders in proportion to the respective amounts described in this clause Fourth held by them;

Fifth, to the payment of all other Secured Obligations of the Loan Parties that are due and payable to the Agents and the other Secured Parties on such date, ratably based upon the respective aggregate amounts of all such Secured Obligations owing to the Agents and the other Secured Parties on such date; and

Finally, after the full and final payment in Cash of all of the Secured Obligations (other than inchoate obligations), to any creditor holding a junior Lien on the Collateral, or to the Loan Parties or each of their representatives or as a court of competent jurisdiction may direct.

Agent shall be deemed to have acted reasonably in the custody, preservation and disposition of any of the Collateral if it complies with the obligations of a secured party under the UCC.

10.3 No Waiver. Agent shall be under no obligation to marshal any of the Collateral for the benefit of the Loan Parties or any other Person, and each Loan Party expressly waives all rights, if any, to require Agent to marshal any Collateral.

10.4 Pledged Collateral. Upon the occurrence and during the continuation of an Event of Default, (a) at Agent's election and upon written notice to the applicable Loan Party, Agent may vote any or all Equity Interests (whether or not the same shall have been transferred into its name or the name of its nominee or nominees) for any lawful purpose, including, without limitation, for the liquidation of the assets of the issuer thereof, and give all consents, waivers and ratifications in respect of the Equity Interests and otherwise act with respect thereto as though it were the outright owner thereof (hereby irrevocably constituting and appointing Agent the proxy and attorney-in-fact of such Loan Party, with full power of substitution, to do so); (b) Agent may demand, sue for, collect or make any compromise or settlement Agent deems suitable in respect of any Equity Interests; (c) Agent may sell, resell, assign and deliver, or otherwise dispose of any or all of the Pledged Collateral, for Cash or credit or both and upon such terms at such place or places, at such time or times and to such entities or other persons as Agent deems expedient, all without demand for performance by any Loan Party or any notice or advertisement whatsoever except as expressly provided herein or as may otherwise be required by law; (d) Agent may cause all or any part of the Pledged Collateral to be transferred into its name or the name of its nominee or nominees; and (e) at Agent's election and upon written notice thereof to the applicable Loan Party, Agent may exercise all membership or partnership, as applicable, rights, powers and privileges to the same extent as the applicable Loan Party is entitled to exercise such rights, powers and privileges. Agent may enforce its rights hereunder without any other notice and without compliance with any other condition precedent now or hereunder imposed by statute, rule of law or otherwise (all of which are hereby expressly waived by each Loan Party, to the fullest extent permitted by law). Each Loan Party recognizes that Agent may be unable to effect a public sale or other Disposition of its Equity Interests by reason of certain prohibitions contained in securities laws and other applicable laws, but may be compelled to resort to one or more private sales thereof to a restricted group of purchasers. Each Loan Party agrees that any such private sales may be at prices and other terms less favorable to the seller than if sold at public sales and that such private sales shall not by reason thereof be deemed not to have been made in a commercially reasonable manner. Agent shall be under no obligation to delay a sale of any of the Pledged Collateral for the period of time necessary to permit the issuer of Equity Interests to register such securities for public sale under securities laws or other applicable laws, even if such issuer would agree to do so. In connection with the sale of Pledged Collateral by Agent during the continuation of an Event of Default, each Loan Party agrees to use its commercially reasonable efforts to cause each issuer of the Equity Interests contemplated to be sold, to execute and deliver, and cause the directors and officers of such issuer to execute and deliver, all at such Loan Party's expense, all such instruments and documents, and to do or cause to be done all such other acts and things as may be necessary or, in the reasonable opinion of Agent or the Required Lenders, advisable to exempt such Equity Interests from registration under the provisions of applicable laws, and to make all amendments to such instruments and documents which, in the opinion of Agent or the Required Lenders, are necessary or advisable, all in conformity with the requirements of applicable laws and the rules and regulations of the Securities and Exchange Commission applicable thereto.

10.5 Cumulative Remedies. The rights, powers and remedies of Agents hereunder shall be in addition to all rights, powers and remedies given by statute or rule of law and are cumulative. The exercise of any one or more of the rights, powers and remedies provided herein shall not be construed as a waiver of or election of remedies with respect to any other rights, powers and remedies of Agents.

SECTION 11.<u>MISCELLANEOUS</u>

11.1 Severability. Whenever possible, each provision of this Agreement shall be interpreted in such manner as to be effective and valid under applicable law, but if any provision of this Agreement shall be prohibited by or invalid under such law, such provision shall be ineffective only to the extent and duration of such prohibition or invalidity, without invalidating the remainder of such provision or the remaining provisions of this Agreement.

11.2 Notice. Except as otherwise provided herein, any notice, demand, request, consent, approval, declaration, service of process or other communication (including the delivery of Financial Statements) that is required, contemplated, or permitted under the Loan Documents or with respect to the subject matter hereof shall be in writing, and shall be deemed to have been validly served, given, delivered, and received upon the earlier of: (i) the day of transmission by electronic mail or hand delivery or delivery by an overnight express service or overnight mail delivery service; or (ii) the third calendar day after deposit in the United States of America mails, with proper first class postage prepaid, in each case addressed to the party to be notified as follows:

(a) If to Administrative Agent:

U.S. Bank National Association, as Administrative Agent

c/o Corporate Trust – CDO Loan Agency

Attention: [***]

214 N. Tryon Street

27th Floor

Charlotte, NC 28202

email: [***]

Telephone: [***]

(b) If to Collateral Agent:

U.S. Bank National Association, as Collateral Agent

Global Corporate Trust

1 Federal St.

Boston, MA 02110

EX-MA-FED

Attention: [***]

email: [***]

Telephone: [***]

(c) If to any Loan Party:

c/o BridgeBio Pharma, Inc.

421 Kipling Street

Palo Alto, CA 94301

email: [***]

Telephone: [***]

or to such other address as each party (including any Lender) may designate for itself by like notice.

11.3 Entire Agreement; Amendments.

(a) This Agreement and the other Loan Documents constitute the entire agreement and understanding of the parties hereto in respect of the subject matter hereof and thereof, and supersede and replace in their entirety any prior proposals, term sheets, non-disclosure or confidentiality agreements, letters, negotiations or other documents or agreements, whether written or oral, with respect to the subject matter hereof or thereof.

(b) Neither this Agreement, any other Loan Document, nor any terms hereof or thereof may be amended, supplemented or modified except in accordance with the provisions of this

Section 11.3(b). The Required Lenders and each Loan Party to the relevant Loan Document may, or, with the written consent of the Required Lenders, Agent and the Loan Parties party to the relevant Loan Document may, from time to time, (i) enter into written amendments, supplements or modifications hereto and to the other Loan Documents for the purpose of adding any provisions to this Agreement or the other Loan Documents or changing in any manner the rights of Lender or of the Loan Parties hereunder or thereunder or (ii) waive, on such terms and conditions as the Required Lenders or Agent, as the case may be, may specify in such instrument, any of the requirements of this Agreement or the other Loan Documents or any Default or Event of Default and its consequences; provided, however, that no such waiver and no such amendment, supplement or modification shall (A) forgive or reduce the principal amount or extend the final scheduled date of maturity of any Loan, extend the scheduled date of or reduce the amount of any amortization payment in respect of any Term Loan Advance, reduce the stated rate of any interest or reduce the amount of or waive or forgive any fee payable hereunder or under the Fee Letters, or extend the scheduled date of any payment thereof, in each case without the written consent of each Lender directly affected thereby; (B) eliminate or reduce the voting rights of any Lender under this Section 11.3(b) without the written consent of each Lender directly affected thereby; (C) reduce any percentage specified in, or otherwise amend, the definition of Required Lenders, consent to the assignment or transfer by the Loan Parties of any of their rights and obligations under this Agreement and the other Loan Documents, release all or substantially all of the Collateral or, other than as expressly permitted hereunder, release a material portion of the Collateral or release a Loan Party from its obligations under the Loan Documents, in each case without the written consent of all Lenders; (D) extend or increase or, other than as expressly permitted hereunder, decrease the commitments to advance funds (including any Tranche I Term Commitment and Tranche II Term Commitment) of any Lender without the written consent of such Lender or extend the Delayed Draw Expiration Date or waive or modify the conditions to making a Tranche II Advance, in each case without the written consent of each Lender holding a Tranche II Term Commitment; (E) subordinate the Secured Obligations (in right of payment or security, including the priority of Liens securing the Secured Obligations) under the Loan Documents to any other Indebtedness (other than to Permitted Senior Debt solely to the extent expressly permitted hereunder) without the written consent of each Lender adversely affected thereby; (F) modify Section 2.7, the payment waterfall under Section 10.2 or any other provision in the Loan Documents relating to pro rata sharing of payments without the written consent of each Lender adversely affected thereby; or (G) amend, modify or waive any provision of Section 11.17 or any other provision adversely affecting Agent without the written consent of Agent. Any such waiver and any such amendment, supplement or modification shall apply equally to each Lender and shall be binding upon the Loan Parties, Lender, Agent and all future holders of the Loans.

Notwithstanding anything herein to the contrary, no Defaulting Lender shall have any right to approve or disapprove any amendment, waiver or consent hereunder, any Defaulting Lender shall be excluded in determining whether all Lenders, all affected Lenders or the Required Lenders have taken or may take any action hereunder (including any consent to any amendment or waiver pursuant to this Section 11.3); and any amendment, waiver or consent that by its terms requires the consent of all the Lenders or each affected Lender may be effected with the consent of the applicable Lenders other than Defaulting Lenders, except that (x) the Term Commitment of any Defaulting Lender may not be increased or extended, or the maturity of any of its Loan may not be extended, the rate of interest on any of its Loans may not be reduced and the principal amount of any of its Loans may not be forgiven, in each case without the consent of such Defaulting Lender and (y) any amendment, waiver or consent requiring the consent of all the Lenders or each affected Lender that by its terms affects any Defaulting Lender more adversely than the other affected Lenders shall require the consent of such Defaulting Lender.

11.4 No Strict Construction. The parties hereto have participated jointly in the negotiation and drafting of this Agreement. In the event an ambiguity or question of intent or interpretation arises, this Agreement shall be construed as if drafted jointly by the parties hereto and no presumption or burden of proof shall arise favoring or disfavoring any party by virtue of the authorship of any provisions of this Agreement.

11.5 No Waiver. The powers conferred upon Agent and Lenders by this Agreement are solely to protect its rights hereunder and under the other Loan Documents and its interest in the Collateral and shall not impose any duty upon Agent or Lenders to exercise any such powers. No omission or delay by Agent or Lenders at any time to enforce any right or remedy reserved to it, or to require performance of any of the terms, covenants or provisions hereof by the Loan Parties at any time designated, shall be a waiver of any such right or remedy to which Agent or Lenders is entitled, nor shall it in any way affect the right of Agent or Lenders to enforce such provisions thereafter.

11.6 Survival. All agreements, representations and warranties contained in this Agreement and the other Loan Documents or in any document delivered pursuant hereto or thereto shall be for the benefit of Agent and Lenders and shall survive the execution and delivery of this Agreement. Sections 2.8, 6.3, 11.11 and Section 11.14 shall survive the termination of this Agreement.

11.7 Successors and Assigns; Participations. The provisions of this Agreement and the other Loan Documents shall inure to the benefit of and be binding on each Loan Party and its permitted assigns (if any). No Loan Party shall assign its obligations under this Agreement or any of the other Loan Documents without Agent's express prior written consent (as directed by the Required Lenders), and any such attempted assignment shall be void and of no effect. Any Lender may assign, transfer, or endorse its rights hereunder and under the other Loan Documents without prior notice to the Loan Parties (other than to a Disqualified Institution or to a Defaulting Lender), and all of such rights shall inure to the benefit of such Lender's successors and assigns; provided that as long as no Default or Event of Default has occurred and is continuing, no Lender may assign, transfer or endorse its rights hereunder or under the Loan Documents to any party that is a Disqualified Institution or Defaulting Lender, it being acknowledged that in all cases, any transfer to a Controlled Investment Affiliate of any Lender shall be allowed; provided that, notwithstanding anything to the contrary herein, until the first anniversary of the Closing Date, no Lender shall assign, transfer or endorse its rights hereunder or under the Loan Documents to any Person other than such Lender's Affiliates and any other Lender party hereto. Agent, acting solely for this purpose as an agent of the Loan Parties, shall maintain at one of its offices in the State of New York a copy of each assignment delivered to it in connection with any assignment by a Lender, and a register for the recordation of the names and addresses of each Lender, and the Term Commitments of, and principal amounts (and stated interest) of the Loans owing to, each Lender pursuant to the terms hereof from time to time (the "Register"). The entries in the Register shall be conclusive absent manifest error, and the Loan Parties, Agent and Lender shall treat each Person whose name is recorded in the Register pursuant to the terms hereof as Lender hereunder for all purposes of this Agreement. The Register shall be available for inspection by the Loan Parties and Lender, at any reasonable time and from time to time upon reasonable prior notice.

In the event that any Lender sells participations in a Loan, such Lender shall, acting for this purpose as a non-fiduciary agent on behalf of the Borrower, maintain, or cause to be maintained, a register, on which it enters the name of all participants in the Registered Loans held by it and the principal amount (and stated interest thereon) of the portion of the Registered Loan that is the subject of the participation (the "Participant Register"). A Registered Loan (and the registered note, if any, evidencing the same) may be participated in whole or in part only by registration of such participation on the Participant Register (and each registered note shall expressly so provide). Any participation of such Loan (and the registered note, if any, evidencing the same) may be effected only by the registration of such participation on the Participant Register. The Participant Register shall be available for inspection by Borrower and any Lender at any reasonable time and from time to time upon reasonable prior notice.

Each Lender may sell participations to one or more banks or other entities in or to all or a portion of its rights and obligations under this Agreement and the other Loan Documents (including, without limitation, all or a portion of its Term Commitments and the Loans made by it); provided, that (i) such Lender's obligations under this Agreement (including without limitation, its Term Commitments hereunder) and the other Loan Documents shall remain unchanged; (ii) such Lender shall remain solely responsible to the other parties hereto for the performance of such obligations, and Borrower, the Agent and the Lenders shall continue to deal solely and directly with such Lender in connection with such Lender's rights and obligations under this Agreement and the other Loan Documents; and (iii) a participant shall not be entitled to require such Lender to take or omit to take any action hereunder except (A) action directly effecting an extension of the maturity dates or decrease in the principal amount of the Loans, (B) action directly effecting an extension of the due dates or a decrease in the rate of interest payable on the Loans or the fees payable under this Agreement or under the Fee Letters, or (C) actions directly effecting a release of all or a substantial portion of the Collateral or any Loan Party (except as otherwise permitted under this Agreement or any other Loan Document). The Loan Parties agree that each participant shall be entitled to the benefits of Section 2.8 (subject to the requirements and limitations therein, including the requirements under Section 2.8(d) (it being understood that the documentation required under Section 2.8(d) shall be delivered to the participating Lender)) to the same extent as if it were a Lender and had acquired its interest by assignment pursuant this Section 11.7; provided that such participant shall not be entitled to receive any greater payment under Section 2.8, with respect to any participation, than its participating Lender would have been entitled to receive, except to the extent such entitlement to receive a greater payment results from a Change in Law that occurs after the participant acquired the applicable participation.

Any Lender may at any time pledge or assign a security interest in all or any portion of its rights under this Agreement to secure obligations of such Lender, including any pledge or assignment to secure obligations to a Federal Reserve Bank or loans made to such Lender pursuant to securitization or similar credit facility (a "Securitization"); provided that no such pledge or assignment shall release such Lender from any of its obligations hereunder or substitute any such pledgee or assignee for such Lender as a party hereto. The Loan Parties shall cooperate with such Lender and its Affiliates to effect the Securitization including, without limitation, by providing such information as may be reasonably requested by such Lender in connection with the rating of its Loans or the Securitization.

The list of Disqualified Institutions will be available to the Lenders upon written request to the Borrower and the Agent, including in connection with an assignment or participation. The parties to this Agreement hereby acknowledge and agree that the Agent will not be deemed to be in default under this Agreement or to have any duty or responsibility or to incur any liabilities as a result of a breach of this paragraph, nor will the Agent have any duty, responsibility or liability to monitor or enforce assignments, participations or other actions in respect of Disqualified Institutions, or otherwise take (or omit to take) any action with respect thereto.

In connection with any assignment of rights and obligations of any Defaulting Lender hereunder, no such assignment shall be effective unless and until, in addition to the other conditions thereto set forth herein, the parties to the assignment shall make such additional payments to the Agent in an aggregate amount sufficient, upon distribution thereof as appropriate (which may be outright payment, purchases by the assignee of participations or subparticipations, or other compensating actions, including funding, with the consent of Borrower and the Agent, the applicable pro rata share of Term Loan Advances previously requested but not funded by the Defaulting Lender, to each of which the applicable assignee and assignor hereby irrevocably consent), to (x) pay and satisfy in full all payment liabilities then owed by such Defaulting Lender to the Agent and each other Lender hereunder (and interest accrued thereon), and (y) acquire (and fund as appropriate) its full pro rata share of all Term Loan Advances in accordance with its pro rata share thereof. Notwithstanding the foregoing, in the event that any assignment of rights and obligations of any Defaulting Lender hereunder shall become effective under applicable law without compliance with the provisions of this paragraph, then the assignee of such interest shall be deemed to be a Defaulting Lender for all purposes of this Agreement until such compliance occurs.

11.8 Governing Law. This Agreement and the other Loan Documents have been negotiated and delivered to Agents and the Lenders in the State of New York, and shall have been accepted by Agent and the Lenders in the State of New York. This Agreement and the other Loan Documents shall be governed by, and construed and enforced in accordance with, the laws of the State of New York, excluding conflict of laws principles that would cause the application of laws of any other jurisdiction.

11.9 Consent to Jurisdiction and Venue. All judicial proceedings (to the extent that the reference requirement of Section 11.10 is not applicable) arising in or under or related to this Agreement or any of the other Loan Documents may be brought in any state or federal court located in the State of New York. By execution and delivery of this Agreement, each party hereto generally and unconditionally: (a) consents to nonexclusive personal jurisdiction in the State and County of New York, Borough of Manhattan; (b) waives any objection as to jurisdiction or venue in the State and County of New York, Borough of Manhattan; (c) agrees not to assert any defense based on lack of jurisdiction or venue in the aforesaid courts; and (d) irrevocably agrees to be bound by any judgment rendered thereby in connection with this Agreement or the other Loan Documents following the exhaustion of all rights with respects to appeals relating thereto. Service of process on any party hereto in any action arising out of or relating to this Agreement shall be effective if given in accordance with the requirements for notice set forth in Section 11.2 and shall be deemed effective and received as set forth in Section 11.2. Nothing herein shall affect the right to serve process in any other manner permitted by law or shall limit the right of either party to bring proceedings in the courts of any other jurisdiction.

11.10 Mutual Waiver of Jury Trial / Judicial Reference.

(a) Because disputes arising in connection with complex financial transactions are most quickly and economically resolved by an experienced and expert Person and the parties wish applicable state and federal laws to apply (rather than arbitration rules), the parties desire that their disputes be resolved by a judge applying such applicable laws. EACH OF THE LOAN PARTIES, AGENT AND THE LENDERS SPECIFICALLY WAIVES ANY RIGHT IT MAY HAVE TO TRIAL BY JURY OF ANY CAUSE OF ACTION, CLAIM, CROSS-CLAIM, COUNTERCLAIM, THIRD PARTY CLAIM OR ANY OTHER CLAIM (COLLECTIVELY, "CLAIMS") ASSERTED BY THE LOAN PARTIES AGAINST AGENT, ANY LENDER OR THEIR RESPECTIVE ASSIGNEE OR BY AGENT, ANY LENDER OR THEIR RESPECTIVE

ASSIGNEE AGAINST ANY LOAN PARTY. This waiver extends to all such Claims, including Claims that involve Persons other than Agent, the Loan Parties and Lenders; Claims that arise out of or are in any way connected to the relationship among the Loan Parties, Agent and Lenders; and any Claims for damages, breach of contract, tort, specific performance, or any equitable or legal relief of any kind, arising out of this Agreement or any other Loan Document.

(b) In the event Claims are to be resolved by judicial reference, either party may seek from a court identified in Section 11.9, any prejudgment order, writ or other relief and have such prejudgment order, writ or other relief enforced to the fullest extent permitted by law notwithstanding that all Claims are otherwise subject to resolution by judicial reference.

11.11 Professional Fees. Each Loan Party promises to pay Agents' and each Lender's reasonable and documented out-of-pocket fees and expenses necessary to finalize the loan documentation, including but not limited to reasonable attorneys' fees, UCC searches, filing costs, and other miscellaneous expenses. In addition, each Loan Party promises to pay any and all reasonable and documented out-of-pocket attorneys' and other professionals' fees and expenses incurred by Agent and each Lender after the Closing Date in connection with or related to: (a) the Loan; (b) the administration, collection, or enforcement of the Loan; (c) the amendment or modification of the Loan Documents; (d) any waiver, consent, release, or termination under the Loan Documents; (e) the protection, preservation, audit, field exam, sale, lease, liquidation, or disposition of Collateral or the exercise of remedies with respect to the Collateral; (f) any legal, litigation, administrative, arbitration, or out of court proceeding in connection with or related to the Loan Parties or the Collateral, and any appeal or review thereof; and (g) any bankruptcy, restructuring, reorganization, assignment for the benefit of creditors, workout, foreclosure, or other action related to the Loan Parties, the Collateral, the Loan Documents, including representing Agent or any Lender in any adversary proceeding or contested matter commenced or continued by or on behalf of any Loan Party's estate, and any appeal or review thereof. This Section 11.11 shall survive and remain in full force and effect regardless of the resignation or removal of any Agent or the termination of this Agreement.

11.12 Confidentiality. Agents and each Lender acknowledge that certain items of Collateral and information provided to Agents and each Lender by the Loan Parties are confidential and proprietary information of the Loan Parties, if and to the extent such information either (i) is marked as confidential by the Loan Parties at the time of disclosure, or (ii) should reasonably be understood to be confidential (the "Confidential Information"). Accordingly, Agents and Lenders agree that any Confidential Information it may obtain in the course of acquiring, administering, or perfecting Agent's security interest in the Collateral shall not be disclosed to any other Person or entity in any manner whatsoever, in whole or in part, without the prior written consent of the Loan Parties, except that Agent and Lenders may disclose any such information: (a) to its own directors, officers, employees, accountants, counsel and other professional advisors and to its Affiliates if Agent or any Lender in their reasonable discretion determines that any such party should have access to such information in connection with such party's responsibilities in connection with the Loan or this Agreement and, provided that such recipient of such Confidential Information either (i) agrees to be bound by the confidentiality provisions of this paragraph or (ii) is otherwise subject to confidentiality restrictions that reasonably protect against the disclosure of Confidential Information; (b) if such information is generally available to the public (other than a result of a breach of this Section); (c) if required or appropriate in any report, statement or testimony submitted to any governmental authority having or claiming to have jurisdiction over Agent or the applicable Lender; (d) if required or appropriate in response to any summons or subpoena or in connection with any litigation, to the extent permitted or deemed advisable by Agent's or Lender's counsel; (e) to comply with any legal requirement or law applicable to Agent or such Lender; (f) to the extent reasonably necessary in connection with the exercise of any right or remedy under any Loan Document, including Agent's sale, lease, or other Disposition of Collateral after Default; (g) to any participant or assignee of Agent or such Lender or any prospective participant or assignee; provided, that such participant or assignee or prospective participant or assignee agrees in writing to be bound by this Section prior to disclosure; or (h) otherwise with the prior consent of the Loan Parties; provided, that any disclosure made in violation of this Agreement shall not affect the obligations of the Loan Parties or any of their respective Affiliates or any guarantor under this Agreement or the other Loan Documents. Agent's and each Lender's respective obligations under this Section 11.12 shall supersede and replace in their entirety the confidentiality provisions of any prior proposals, term sheets, non-disclosure or confidentiality agreements with respect to the subject matter hereof or thereof.

11.13 Assignment of Rights. Each Loan Party acknowledges and understands that any Lender may, subject to Section 11.7, sell and assign all or part of its interest hereunder and under the Loan Documents to any Person or entity (an "Assignee"). The parties to each such assignment shall execute and deliver to the Administrative Agent an Assignment and Assumption, substantially in the form of Exhibit H, together, in each case, with a processing and recordation fee of $3,500 (which fee may be waived or reduced in the sole discretion of the Administrative Agent.) After such assignment the term "Lender" as used in the Loan Documents shall mean and include such Assignee, and such Assignee shall be vested with all rights, powers and remedies of a Lender hereunder with respect to the interest so assigned; but with respect to any such interest not so transferred, Lender shall retain all rights, powers and remedies hereby given. No such assignment by any Lender shall relieve any Loan Party of any of its obligations hereunder. Each Lender agrees that in the event of any transfer by it of the Term Note(s) (if any), it will endorse thereon a notation as to the portion of the principal of the Term Note(s), which shall have been paid at the time of such transfer and as to the date to which interest shall have been last paid thereon.

11.14 Revival of Secured Obligations; Termination. This Agreement and the Loan Documents shall remain in full force and effect and continue to be effective if any petition is filed by or against any Loan Party for liquidation or reorganization, if any Loan Party becomes insolvent or makes an assignment for the benefit of creditors, if a receiver or trustee is appointed for all or any significant part of any Loan Party's assets, or if any payment or transfer of Collateral is recovered from Agent or any Lender. The Loan Documents and the Secured Obligations and Collateral security shall continue to be effective, or shall be revived or reinstated, as the case may be, if at any time payment and performance of the Secured Obligations or any transfer of Collateral to Agent, or any part thereof is rescinded, avoided or avoidable, reduced in amount, or must otherwise be restored or returned by, or is recovered from, Agent, any Lender or by any obligee of the Secured Obligations, whether as a "voidable preference," "fraudulent conveyance," or otherwise, all as though such payment, performance, or transfer of Collateral had not been made. In the event that any payment, or any part thereof, is rescinded, reduced, avoided, avoidable, restored, returned, or recovered, the Loan Documents and the Secured Obligations (other than obligations that survive termination) shall be deemed, without any further action or documentation, to have been revived and reinstated except to the extent of the full, final, and payment in cash to Agent or Lenders in cash. This Agreement and the Loan Documents shall terminate on the payment in full in Cash of the Secured Obligations (other than any obligations that specifically survive termination).

11.15 Counterparts. This Agreement and any amendments, waivers, consents or supplements hereto may be executed in any number of counterparts, and by different parties hereto in separate counterparts, each of which when so delivered shall be deemed an original, but all of which counterparts shall constitute but one and the same instrument. Delivery of an executed counterpart of a signature page to this Agreement or any other Loan Document by telecopier shall be effective as delivery of a manually executed counterpart of this Agreement. Delivery of an executed counterpart of a signature page of this Agreement or any other Loan Document by facsimile or electronic (e.g., in "pdf" or "tif" format) transmission shall be as effective as delivery of a manually executed counterpart hereof. For purposes hereof, the words "execution," "execute," "executed," "signed," "signature" and words of like import shall be deemed to include electronic signatures, the electronic matching of assignment terms and contract formulations on electronic platforms, or the keeping of records in electronic form, each of which shall be of the same legal effect, validity or enforceability as a manually executed signature or the use of a paper-based recordkeeping system, as the case may be, to the extent and as provided for in any applicable law, including the Federal Electronic Signatures in Global and National Commerce Act, the New York State Electronic Signatures and Records Act, or any other similar state laws based on the Uniform Electronic Transaction Act (each, a "Signature Law"). Each party hereto and thereto shall be entitled to conclusively rely upon, and shall have no liability with respect to, any faxed, scanned, or photocopied manual signature, or other electronic signature, of any party and shall have no duty to investigate, confirm or otherwise verify the validity or authenticity thereof. The party using digital signatures and electronic methods agrees to assume all risks arising out of the use of using digital signatures and electronic methods to submit communications and/or documents to Agent, including without limitation the risk of Agent acting on unauthorized instructions, and the risk of interception and misuse by third parties. For avoidance of doubt, original manual signatures shall be used for execution or indorsement of writings when required under the UCC or other applicable Signature Law due to the character or intended character of the writings.

11.16 No Third-Party Beneficiaries. No provisions of the Loan Documents are intended, nor will be interpreted, to provide or create any third-party beneficiary rights or any other rights of any kind in any Person other than Agents, the Lenders and the Loan Parties and Indemnified Persons unless specifically provided otherwise herein, and, except as otherwise so provided, all provisions of the Loan Documents will be personal and solely among Agents, the Lenders and the Loan Parties.

11.17 Agency.

(a) Each Lender hereby irrevocably appoints U.S. Bank National Association to act on its behalf as Agent hereunder and under the other Loan Documents (in its respective capacities as Administrative Agent and Collateral Agent, as applicable) and authorizes Agent to take such actions on its behalf and to exercise such powers as are delegated to Agent by the terms hereof or thereof, together with such actions and powers as are reasonably incidental thereto. For the avoidance of doubt, each Lender hereby authorizes and directs Agent to enter into the Account Control Agreement set forth on Schedule 4.1 or other Account Control Agreements with respect to all Deposit Accounts and any accounts where Investment Property is maintained, as required by Section 7.12 hereof.

(b) Each Lender agrees to indemnify Agent in its capacity as such (to the extent not reimbursed by the Loan Parties and without limiting the obligation of the Loan Parties to do so), according to its aggregate percentage of the total Term Commitments plus outstanding Term Loan Advances (based upon the total outstanding Term Commitments plus total outstanding Term Loan Advances) in effect on the date on which indemnification is sought under this Section 11.17, from and against any and all liabilities, obligations, losses, damages, penalties, actions, judgments, suits, costs, expenses or disbursements of any kind whatsoever that may at any time be imposed on, incurred by or asserted against Agent in any way relating to or arising out of, this Agreement, any of the other Loan Documents or any documents contemplated by or referred to herein or therein or the transactions contemplated hereby or thereby or any action taken or omitted by Agent under or in connection with any of the foregoing, including the enforcement of this provision and including, without limitation any obligation of reimbursement or indemnity under the Account Control Agreements. The agreements in this Section shall survive the resignation or replacement of the Agent, the payment of the Loans and all other amounts payable hereunder, the resignation or replacement of any Agent and the termination of this Agreement.

(c) Agent in Its Individual Capacity. The Person serving as Agent hereunder shall, if applicable, have the same rights and powers in its capacity as a Lender as any other Lender and may exercise the same as though it were not Agent and the term "Lender" shall, unless otherwise expressly indicated or unless the context otherwise requires, include each such Person serving as Agent hereunder in its individual capacity.

(d) Exculpatory Provisions. Agent shall have no duties or obligations except those expressly set forth herein and in the other Loan Documents. Without limiting the generality of the foregoing, Agent shall not:

(i) be subject to any fiduciary or other implied duties, regardless of whether any Default or any Event of Default has occurred and is continuing;

(ii) have any duty to take any discretionary action or exercise any discretionary powers, except discretionary rights and powers expressly contemplated hereby or by the other Loan Documents that Agent is required to exercise as directed in writing by one or more Lenders or Required Lenders, as the case may be, and in all cases, it shall be fully justified in failing or refusing to act hereunder or under any other Loan Documents unless it shall (a) receive written instructions from one or more Lenders or Required Lenders, as applicable, specifying the action to be taken and (b) be indemnified to its satisfaction by Lenders against any and all liability and expenses that may be incurred by it by reason of taking or continuing to take any such action, including any action to be taken pursuant to any Account Control Agreements and any landlord agreements or waivers (if any); provided that Agent shall not be required to take any action that, in its opinion or the opinion of its counsel, may expose Agent to liability or that is contrary to any Loan Document or applicable law, including for the avoidance of doubt any action that may be in violation of the automatic stay under any Debtor Relief Law or that may effect a forfeiture, modification or termination of property of a Defaulting Lender in violation of any Debtor Relief Law;

(iii) be required to expend or risk its own funds or provide indemnities in the performance of any of its duties under this Agreement or any other Loan Document or the exercise of any of its rights or power or otherwise incur any financial liability in the performance of its duties or the exercise of any of its rights or powers; and

(iv) except as expressly set forth herein and in the other Loan Documents, have any duty to disclose, and Agent shall not be liable for the failure to disclose, any information relating to the Loan Parties or any of their respective Affiliates that is communicated to or obtained by any Person serving as Agent or any of its Affiliates in any capacity.

(e) Agent shall not be liable for any action taken or not taken by it (i) with the consent or at the request of the requisite Lender or Lenders hereunder or as Agent shall believe in good faith shall be necessary, under the circumstances or (ii) in the absence of its own gross negligence or willful misconduct as determined by a final, non-appealable order of a court of competent jurisdiction.

(f) Agent shall not be responsible for or have any duty to ascertain or inquire into (i) any statement, warranty or representation made in or in connection with this Agreement or any other Loan Document, (ii) the contents of any certificate, report or other document delivered hereunder or thereunder or in connection herewith or therewith, (iii) the performance or observance of any of the covenants, agreements or other terms or conditions set forth herein or therein or the occurrence of any Default or Event of Default, (iv) the validity, enforceability, effectiveness or genuineness of this Agreement, any other Loan Document or any other agreement, instrument or document or (v) the satisfaction of any condition set forth in Section 4 or elsewhere herein, other than to confirm receipt of items expressly required to be delivered to Agent.

(g) Anything herein to the contrary notwithstanding, whenever reference is made in this Agreement or any other Loan Document to any action by, consent, designation, specification, requirement or approval of, notice, request or other communication from, or other direction given or action to be undertaken or to be (or not to be) suffered or omitted by Agent or to any election, decision, opinion, acceptance, use of judgment, expression of satisfaction or other exercise of discretion, rights or remedies to be made (or not to be made) by Agent hereunder or thereunder, it is understood that in all cases Agent shall be acting, giving, withholding, suffering, omitting, taking or otherwise undertaking and exercising the same (or shall not be undertaking and exercising the same) as directed by the Required Lenders or the Lenders, as applicable. Beyond the exercise of reasonable care in the custody of the Collateral in the possession or control of Agent, Agent will not have any duty as to any other Collateral or any income thereon or as to preservation of rights against prior parties or any other rights pertaining thereto. Agent will be deemed to have exercised reasonable care in the custody of the Collateral in its possession if the Collateral is accorded treatment substantially equal to that which it accords its own property, provided, that Agent shall have no obligation or duty to obtain or monitor insurance in respect of the Collateral, and Agent will not be liable or responsible for any loss or diminution in the value of any of the Collateral by reason of the act or omission of any carrier, forwarding agency or other agent or bailee selected by Agent in good faith.

(h) Reliance by Agent. Agent may rely, and shall be fully protected in acting, or refraining to act, upon, any resolution, statement, certificate, instrument, opinion, report, notice, request, consent, order, bond or other paper or document that it has no reason to believe to be other than genuine and to have been signed or presented by the proper party or parties or, in the case of cables, telecopies and telexes, to have been sent by the proper party or parties. In the absence of its gross negligence or willful misconduct, as determined by a final, non-appealable order of a court of competent jurisdiction, Agent may conclusively rely, as to the truth of the statements and the correctness of the opinions expressed therein, upon any certificates or opinions furnished to Agent and conforming to the requirements of this Agreement or any of the other Loan Documents. Agent may consult with counsel, and any opinion or legal advice of such counsel shall be full and complete authorization and protection in respect of any action taken, not taken or suffered by Agent hereunder or under any Loan Documents in accordance therewith. Agent shall have the right at any time to seek instructions concerning the administration of the Collateral from any court of competent jurisdiction. Agent shall not be under any obligation to exercise any of the rights or powers granted to Agent by this Agreement, this Agreement and the other Loan Documents at the request or direction of Lenders or Required Lenders unless Agent shall have been provided by Lenders or Required Lenders, as the case may be, with adequate security and indemnity against the costs, expenses and liabilities that may be incurred by it in compliance with such request or direction.

(i) Subagents. The Agent may perform any and all of its duties and exercise its rights and powers by or through any one or more sub-agents appointed by it. The exculpatory provisions of the preceding subsections of this Section 11.17 shall apply to any such sub-agent of the Agent.

(j) Force Majeure. No Agent shall be responsible or liable for any failure or delay in the performance of its obligations under this Agreement and the other Loan Documents arising out of or caused, directly or indirectly, by circumstances beyond its control, including without limitation, any act or provision of any present or future law or regulation or governmental authority; acts of God; earthquakes; fires; floods; wars; terrorism; civil or military disturbances; sabotage; epidemics; pandemics; riots; interruptions, loss or malfunctions of utilities, computer (hardware or software) or communications service; accidents; labor disputes; acts of civil or military authority or governmental actions; or the unavailability of the Federal Reserve Bank wire or telex or other wire or communication facility, in each case, other than as resulting from its gross negligence or willful misconduct, as determined by a nonappealable order of a court of competent jurisdiction.

(k) Erroneous Payments.

(i) Each Lender hereby agrees that (i) if the Administrative Agent notifies such Lender that the Administrative Agent has determined in its sole discretion that any funds received by such Lender from the Administrative Agent were erroneously transmitted to, or otherwise erroneously or mistakenly received by, such Lender (whether or not known to such Lender) (whether as a payment, prepayment or repayment of principal, interest, fees or otherwise; individually and collectively, an "Erroneous Payment") and demands the return of such Erroneous Payment (or a portion thereof), such Lender shall promptly, but in no event later than [***] thereafter, return to the Administrative Agent the amount of any such Erroneous Payment (or portion thereof) as to which such a demand was made, in same day funds (in the currency so received), together with interest thereon in respect of each day from and including the date such Erroneous Payment (or portion thereof) was received by such Lender to the date such amount is repaid to the Administrative Agent in same day funds at the Federal Funds Rate and (ii) to the extent permitted by applicable law, such Lender shall not assert any right or claim to the Erroneous Payment, and hereby waives any claim, counterclaim, defense or right of set-off or recoupment with respect to any demand claim or counterclaim by the Administrative Agent for the return of any Erroneous Payments received, including without limitation a waiver of any defense based on "discharge for value" or any similar doctrine. A notice of the Administrative Agent to any Lender under this clause shall be conclusive absent manifest error.

(ii) Without limiting immediately preceding clause, each Lender hereby further agrees that if it receives an Erroneous Payment from Administrative Agent (x) that is in a different amount than, or on a different date from, that specified in a notice of payment sent by the Administrative Agent with respect to such Erroneous Payment (an "Erroneous Payment Notice"), (y) that was not preceded or accompanied by an Erroneous Payment Notice, or (z) that such Lender otherwise becomes aware was transmitted, or received, in error or by mistake (in whole or in part), in each case, an error has been made (and that it is deemed to have knowledge of such error at the time of receipt of such Erroneous Payment) with respect to such Erroneous Payment, and to the extent permitted by applicable law, such Lender shall not assert any right or claim to the Erroneous Payment, and hereby waives, any claim, counterclaim, defense or right of set-off or recoupment with respect to any demand, claim or counterclaim by the Administrative Agent for the return of any Erroneous Payments received, including without limitation, waiver of any defense based on "discharge for value" or any similar doctrine. Each Lender agrees that, in each such case, it shall promptly (and, in all events, within [***] of its knowledge (or deemed knowledge) of such error) notify the Administrative Agent of such occurrence and, upon demand from the Administrative Agent, it shall promptly, but in all events no later than [***] thereafter, return to the Administrative Agent the amount of any such Erroneous Payment (or portion thereof) as to which such a demand was made in same day funds (in the currency so received), together with interest thereon in respect of each day from and including the date such Erroneous Payment (or portion thereof) was received by such Lender to the date such amount is repaid to the Administrative Agent in same day funds at the greater of the Federal Funds Rate and a rate determined by the Administrative Agent in accordance with banking industry rules on interbank compensation from time to time in effect.

(iii) For purposes of this clause, "Federal Funds Rate" means, for any day, the rate per annum equal to the weighted average of the rates on overnight Federal funds transactions with members of the Federal Reserve System on such day, as published by the Federal Reserve Bank of New York on the Business Day next succeeding such day; provided that if such day is not a Business Day, the Federal Funds Effective Rate for such day shall be such rate on such transactions on the preceding Business Day as so published on the next succeeding Business Day.

(l) Resignation and Replacement of Agents.

(i) Each Agent may at any time give notice of its resignation to the Lender and the Borrower. Upon receipt of any such notice of resignation, the Required Lenders shall have the right, in consultation with the Borrower, to appoint a successor. If no such successor shall have been so appointed by the Required Lenders and shall have accepted such appointment within [***] after the retiring Agent gives notice of its resignation (or such earlier day as shall be agreed by the Required Lenders) (the "Resignation Effective Date"), then the retiring Agent may (but shall not be obligated to), on behalf of the Lender, appoint a successor Agent meeting the qualifications set forth above; provided that in no event shall any such successor Agent be a Defaulting Lender. Whether or not a successor has been appointed, such resignation shall become effective in accordance with such notice on the Resignation Effective Date.

(ii) If the Person serving as Agent is a Defaulting Lender pursuant to clause (d) of the definition thereof, the Required Lenders may, to the extent permitted by applicable law, by notice in writing to the Borrower and such Person removes such Person as Agent and, in consultation with the Borrower, appoint a successor. If no such successor shall have been so appointed by the Required Lenders and shall have accepted such appointment within [***] (or such earlier day as shall be agreed by the Required Lenders) (the "Removal Effective Date"), then such removal shall nonetheless become effective in accordance with such notice on the Removal Effective Date.

(iii) With effect from the Resignation Effective Date or the Removal Effective Date (as applicable) (i) the retiring or removed Agent shall be discharged from its duties and obligations hereunder and under the other Loan Documents and (ii) except for any fees, expenses and indemnity payments owed to the retiring or removed Agent, all payments, communications and determinations provided to be made by, to or through the Agent shall instead be made by or to each Lender directly, until such time, if any, as the Required Lenders appoint a successor Agent as provided for above. Upon the acceptance of a successor's appointment as Agent hereunder, such successor shall succeed to and become vested with all of the rights, powers, privileges and duties of the retiring or removed Agent (other than any rights to fees, expenses and indemnity payments owed to the retiring or removed Agent), and the retiring or removed Agent shall be discharged from all of its duties and obligations hereunder or under the other Loan Documents. The fees payable by the Borrower to a successor Agent shall be the same as those payable to its predecessor unless otherwise agreed between the Borrower and such successor. After the retiring or removed Agent's resignation or removal hereunder and under the other Loan Documents, the provisions of this Article shall continue in effect for the benefit of such retiring or removed Agent, its sub agents and their respective Related Parties in respect of any actions taken or omitted to be taken by any of them while the retiring or removed Agent was acting as Agent.

11.18 Publicity. None of the parties hereto nor any of its respective member businesses and Affiliates shall, without the other parties' prior written consent (which shall not be unreasonably withheld or delayed), publicize or use (a) the other party's name (including a brief description of the relationship among the parties hereto), logo or hyperlink to such other parties' web site, separately or together, in written and oral presentations, advertising, promotional and marketing materials, client lists, public relations materials or on its web site (together, the "Publicity Materials"); (b) the names of officers of such other parties in the Publicity Materials; and (c) such other parties' name, trademarks, servicemarks in any news or press release concerning such party; provided however, notwithstanding anything to the contrary herein, no such consent shall be required (i) to the extent necessary to comply with the requests of any regulators, legal requirements or laws applicable to such party (including, without limitation, the public reporting requirements of the Securities and Exchange Commission), pursuant to any listing agreement with any national securities exchange (so long as such party provides prior notice to the other party hereto to the extent reasonably practicable) and (ii) to comply with Section 11.12.

11.19 Multiple Loan Parties.

(a) Loan Parties' Agent. Each Loan Party hereby irrevocably appoints Borrower as its agent, attorney-in-fact and legal representative for all purposes, including requesting disbursement of the Term Loan Advance and receiving account statements and other notices and communications to the Loan Parties (or any of them) from Agent or any Lender. Agent may rely, and shall be fully protected in relying, on any request for the Term Loan Advance, disbursement instruction, report, information or any other notice or communication made or given by Borrower, whether in its own name or on behalf of one or more of the other Loan Parties, and Agent shall not have any obligation to make any inquiry or request any confirmation from or on behalf of any other Loan Party as to the binding effect on it of any such request, instruction, report, information, other notice or communication, nor shall the joint and several character of Loan Parties' obligations hereunder be affected thereby.

(b) Waivers. Each Loan Party hereby waives: (i) any right to require Agent to institute suit against, or to exhaust its rights and remedies against, any other Loan Party or any other Person, or to proceed against any property of any kind which secures all or any part of the Secured Obligations, or to exercise any right of offset or other right with respect to any reserves, credits or deposit accounts held by or maintained with Agent or any Indebtedness of Agent or any Lender to any other Loan Party, or to exercise any other right or power, or pursue any other remedy Agent or any Lender may have; (ii) any defense arising by reason of any disability or other defense of any other Loan Party or any endorser, co-maker or other Person, or by reason of the cessation from any cause whatsoever of any liability of any other Loan Party or any endorser, co-maker or other Person, with respect to all or any part of the Secured Obligations, or by reason of any act or omission of Agent or others which directly or indirectly results in the discharge or release of any other Loan Party or any other Person or any Secured Obligations or any security therefor, whether by operation of law or otherwise; (iii) any defense arising by reason of any failure of Agent to obtain, perfect, maintain or keep in force any Lien on, any property of any Loan Party or any other Person; (iv) any defense based upon or arising out of any bankruptcy, insolvency, reorganization, arrangement, readjustment of debt, liquidation or dissolution proceeding commenced by or against any other Loan Party or any endorser, co-maker or other Person, including without limitation any discharge of, or bar against collecting, any of the Secured Obligations (including without limitation any interest thereon), in or as a result of any such proceeding. Until all of the Secured Obligations have been paid, performed, and discharged in full, nothing shall discharge or satisfy the liability of any Loan Party hereunder except the full performance and payment of all of the Secured Obligations. If any claim is ever made upon Agent for repayment or recovery of any amount or amounts received by Agent in payment of or on account of any of the Secured Obligations, because of any claim that any such payment constituted a preferential transfer or fraudulent conveyance, or for any other reason whatsoever, and Agent repays all or part of said amount by reason of any judgment, decree or order of any court or administrative body having jurisdiction over Agent or any of its property, or by reason of any settlement or compromise of any such claim effected by Agent with any such claimant (including without limitation the any other Loan Party), then and in any such event, each Loan Party agrees that any such judgment, decree, order, settlement and compromise shall be binding upon such Loan Party, notwithstanding any revocation or release of this Agreement or the cancellation of any note or other instrument evidencing any of the Secured Obligations, or any release of any of the Secured Obligations, and each Loan Party shall be and remain liable to Agent and Lenders under this Agreement for the amount so repaid or recovered, to the same extent as if such amount had never originally been received by Agent or any Lender, and the provisions of this sentence shall survive, and continue in effect, notwithstanding any revocation or release of this Agreement. Each Loan Party hereby expressly and unconditionally waives all rights of subrogation, reimbursement and indemnity of every kind against any other Loan Party, and all rights of recourse to any assets or property of any other Loan Party, and all rights to any collateral or security held for the payment and performance of any Secured Obligations, including (but not limited to) any of the foregoing rights which any Loan Party may have under any present or future document or agreement with any other Loan Party or other Person, and including (but not limited to) any of the foregoing rights which any Loan Party may have under any equitable doctrine of subrogation, implied contract, or unjust enrichment, or any other equitable or legal doctrine.

(c) Consents. Each Loan Party hereby consents and agrees that, without notice to or by such Loan Party and without affecting or impairing in any way the obligations or liability of such Loan Party hereunder, Agent may, from time to time before or after revocation of this Agreement, do any one or more of the following (as directed by the Required Lenders in their sole and absolute discretion): (i) accept partial payments of, compromise or settle, renew, extend the time for the payment, discharge, or performance of, refuse to enforce, and release all or any parties to, any or all of the Secured Obligations; (ii) grant any other indulgence to any Loan Party or any other Person in respect of any or all of the Secured Obligations or any other matter; (iii) accept, release, waive, surrender, enforce, exchange, modify, impair, or extend the time for the performance, discharge, or payment of, any and all property of any kind securing any or all of the Secured Obligations or any guaranty of any or all of the Secured Obligations, or on which Agent at any time may have a Lien, or refuse to enforce its rights or make any compromise or settlement or agreement therefor in respect of any or all of such property; (iv) substitute or add, or take any action or omit to take any action which results in the release of, any one or more other Loan Parties or any endorsers of all or any part of the Secured Obligations, including, without limitation one or more parties to this Agreement, regardless of any destruction or impairment of any right of contribution or other right of such Loan Party; (v) apply any sums received from any other Loan Party, any guarantor, endorser, or co-signer, or from the disposition of any Collateral or security, to any Indebtedness whatsoever owing from such Person or secured by such Collateral or security, in such manner and order as Agent determines (as directed by the Required Lenders in their sole discretion), and regardless of whether such Indebtedness is part of the Secured Obligations, is secured, or is due and payable. Each Loan Party consents and agrees that Agent shall be under no obligation to marshal any assets in favor of any Loan Party, or against or in payment of any or all of the Secured Obligations. Each Loan Party further consents and agrees that Agent shall have no duties or responsibilities whatsoever with respect to any property securing any or all of the Secured Obligations. Without limiting the generality of the foregoing, Agent shall have no obligation to monitor, verify, audit, examine, or obtain or maintain any insurance with respect to, any property securing any or all of the Secured Obligations.

(d) Independent Liability. Each Loan Party hereby agrees that one or more successive or concurrent actions may be brought hereon against such Loan Party, in the same action in which any other Loan Party may be sued or in separate actions, as often as deemed advisable by Agent. Each Loan Party is fully aware of the financial condition of each other Loan Party and is executing and delivering this Agreement based solely upon its own independent investigation of all matters pertinent hereto, and such Loan Party is not relying in any manner upon any representation or statement of Agent or any Lender with respect thereto. Each Loan Party represents and warrants that it is in a position to obtain, and each Loan Party hereby assumes full responsibility for obtaining, any additional information concerning any other Loan Party's financial condition and any other matter pertinent hereto as such Loan Party may desire, and such Loan Party is not relying upon or expecting Agent to furnish to it any information now or hereafter in Agent's possession concerning the same or any other matter.

(e) Subordination. All Indebtedness of any Loan Party now or hereafter arising held by another Loan Party is subordinated to the Secured Obligations and any Loan Party holding the Indebtedness shall take all actions reasonably requested by Agent (as directed by the Required Lenders) to effect, to enforce and to give notice of such subordination.

SECTION 12. GUARANTY

12.1 Guaranty. Each Loan Party hereby agrees that such Loan Party is jointly and severally liable for, and hereby absolutely and unconditionally guarantees to each Agent and the Lenders and their respective successors and assigns, the full and prompt payment (whether at stated maturity, by acceleration or otherwise) and performance of, all Secured Obligations owed or hereafter owing to each Agent and the Lenders by each other Loan Party. Each Loan Party agrees that its guaranty obligation hereunder is a continuing guaranty of payment and performance and not of collection, and that its obligations under this Section 12 shall be absolute and unconditional, irrespective of, and unaffected by:

(a) the genuineness, validity, regularity, enforceability or any future amendment of, or change in, this Agreement, any other Loan Document or any other agreement, document or instrument to which any Loan Party is or may become a party;

(b) the absence of any action to enforce this Agreement (including this Section 12) or any other Loan Document or the waiver or consent by Agent and Lenders with respect to any of the provisions thereof;

(c) the existence, value or condition of, or failure to perfect its Lien against, any security for the Secured Obligations or any action, or the absence of any action, by Agent and the Lenders in respect thereof (including the release of any such security);

(d) the insolvency of any Loan Party; or

(e) any other action or circumstances which might otherwise constitute a legal or equitable discharge or defense of a surety or guarantor;

it being agreed by each Loan Party that its obligations under this Section 12 shall not be discharged until the full and final payment in Cash of all of the Secured Obligations (other than contingent indemnity obligations for which no claim is outstanding)). Each Loan Party shall be regarded, and shall be in the same position, as principal debtor with respect to the Secured Obligations guaranteed hereunder.

12.2 Waivers by the Loan Parties. Each Loan Party expressly waives all rights it may have now or in the future under any statute, or at common law, or pursuant to any other laws or in equity, or otherwise, to compel Agent or the Lenders to marshal assets or to proceed in respect of the Secured Obligations guaranteed hereunder against any other Loan Party, any other party or against any security for the payment and performance of the Secured Obligations before proceeding against, or as a condition to proceeding against, such Loan Party. It is agreed among each Loan Party, Agents and the Lenders that the foregoing waivers are of the essence of the transaction contemplated by this Agreement and the other Loan Documents and that, but for the provisions of this Section 12 and such waivers, Agents and the Lenders would decline to enter into this Agreement.

12.3 Benefit of Guaranty. Each Loan Party agrees that the provisions of this Section 12 are for the benefit of Agent and the Lenders and their respective successors, transferees, endorsees and assigns, and nothing herein contained shall impair, as between Borrower, on the one hand, and Agent and the Lenders, on the other hand, the obligations of such other Loan Party under the Loan Documents.

12.4 Subordination of Subrogation, Etc. Notwithstanding anything to the contrary in this Agreement or in any other Loan Document, and except as set forth in Section 12.7, each Loan Party hereby expressly and irrevocably subordinates to the prior payment in full, in Cash, of the Secured Obligations (other than contingent indemnity obligations for which no claim is outstanding) any and all rights pursuant to any laws or in equity to subrogation, reimbursement, exoneration, contribution, indemnification or set off and any and all defenses available to a surety, guarantor or accommodation co-obligor until the full and final payment in Cash of all of the Secured Obligations (other than contingent indemnity obligations for which no claim is outstanding). Each Loan Party acknowledges and agrees that this subordination is intended to benefit Agent and the Lenders and shall not limit or otherwise affect such Loan Party's liability hereunder or the enforceability of this Section 12, and that Agent, the Lenders and their respective successors and assigns are intended third party beneficiaries of the waivers and agreements set forth in this Section 12.4.

12.5 Election of Remedies. If Agent or any Lender may, under applicable law, proceed to realize its benefits under any of the Loan Documents giving Agent or such Lender a Lien upon any Collateral, whether owned by any Loan Party or by any other Person, either by judicial foreclosure or by non-judicial sale or enforcement, Agent or any Lender may, at its sole option, determine which of its remedies or rights it may pursue without affecting any of its rights and remedies under this Section 12. If, in the exercise of any of its rights and remedies, Agent or any Lender shall forfeit any of its rights or remedies, including its right to enter a deficiency judgment against any Loan Party or any other Person, whether because of any applicable laws pertaining to "election of remedies" or the like, each Loan Party hereby consents to such action by Agent or such Lender and waives any claim based upon such action, even if such action by Agent or such Lender shall result in a full or partial loss of any rights of subrogation which each Loan Party might otherwise have had but for such action by Agent or such Lender. Any election of remedies which results in the denial or impairment of the right of Agent or any Lender to seek a deficiency judgment against any Loan Party shall not impair any other Loan Party's obligation to pay the full amount of the Secured Obligations. In the event Agent or any Lender shall bid at any foreclosure or trustee's sale or at any private sale permitted by law or the Loan Documents, Agent (either directly or through one or more acquisition vehicles) or such Lender may offset the Secured Obligations against the purchase price of such bid in lieu of accepting cash or other non-cash consideration in connection with such sale or other Disposition. The amount of the successful bid at any such sale, whether Agent, any Lender or any other party is the successful bidder, shall be conclusively deemed to be the fair and reasonably equivalent value of the Collateral and the difference between such bid amount and the remaining balance of the Secured Obligations shall be conclusively deemed to be the amount of the Secured Obligations guaranteed under this Section 12, notwithstanding that any present or future law or court decision or ruling may have the effect of reducing the amount of any deficiency claim to which Agent or any Lender might otherwise be entitled but for such bidding at any such sale.

12.6 Limitation. Notwithstanding any provision herein contained to the contrary, the liability of each Loan Party (other than Borrower) under this Section 12 (which liability is in any event in addition to amounts for which such Loan Party is primarily liable under Section 2) shall be limited to an amount not to exceed as of any date of determination the greater of:

(a) the net amount of all Loans (plus all other Secured Obligations owing in connection therewith) advanced to any other Loan Party under this Agreement and then re-loaned or otherwise transferred to, or for the benefit of, such Loan Party; and

(b) the amount which could be claimed by Agent and the Lenders from such Loan Party under this Section 12 without rendering such claim voidable or avoidable under Section 548 of Chapter 11 of the United States Bankruptcy Code, as amended, or under any applicable state Uniform Fraudulent Transfer Act, Uniform Fraudulent Conveyance Act or similar statute or common law.

The provisions of this Section 12.6 shall be implemented automatically without the need for any amendment, modification, termination or waiver of any provision of this Agreement or any other Loan Document

12.7 Contribution with Respect to Guaranty Obligations.

(a) To the extent that any Loan Party shall make a payment under this Section 12 (such payments, "Guarantor Payments") of all or any of the Secured Obligations (other than Loans made to that Loan Party for which it is primarily liable) which, taking into account all other Guarantor Payments then previously or concurrently made by any other Loan Party, exceeds the amount which such Loan Party would otherwise have paid if each Loan Party had paid the aggregate Secured Obligations satisfied by such Guarantor Payment in the same proportion that such Loan Party's "Allocable Amount" (as defined below) (as determined immediately prior to such Guarantor Payment) bore to the aggregate Allocable Amounts of each of the Loan Parties as determined immediately prior to the making of such Guarantor Payment, then, following the occurrence of the full and final payment in Cash of all of the Secured Obligations (other than inchoate obligations), such Loan Party shall be entitled to receive contribution and indemnification payments from, and be reimbursed by, each other Loan Party for the amount of such excess, pro rata based upon their respective Allocable Amounts in effect immediately prior to such Guarantor Payment.

(b) As of any date of determination, the "Allocable Amount" of any Loan Parties shall be equal to the maximum amount of the claim which could then be recovered from such Loan Parties under this Section 12 without rendering such claim voidable or avoidable under Section 548 of Chapter 11 of the United States Bankruptcy Code, as amended or under any applicable state Uniform Fraudulent Transfer Act, Uniform Fraudulent Conveyance Act or similar statute or common law.

(c) This Section 12.7 is intended only to define the relative rights of Loan Parties and nothing set forth in this Section 12.7 is intended to or shall impair the obligations of Loan Parties, jointly and severally, to pay any amounts as and when the same shall become due and payable in accordance with the terms of this Agreement, including Section 12.1. Nothing contained in this Section 12.7 shall limit the liability of any Loan Party to pay the Loans made directly or indirectly to that Loan Party and accrued interest, fees, expenses and all other Secured Obligations with respect thereto for which such Loan Party shall be primarily liable.

(d) The parties hereto acknowledge that the rights of contribution and indemnification hereunder shall constitute assets of the Loan Party to which such contribution and indemnification is owing.

(e) The rights of the indemnifying Loan Parties against other Loan Parties under this Section 12.7 shall be exercisable upon and after the full and final payment in Cash of all of the Secured Obligations (other than inchoate obligations).

12.8 Liability Cumulative. The liability of Loan Parties under this Section 12 is in addition to and shall be cumulative with all liabilities of each Loan Party to Agent and the Lenders under this Agreement and the other Loan Documents to which such Loan Party is a party or in respect of any Secured Obligations or obligation of any other Loan Party, without any limitation as to amount, unless the instrument or agreement evidencing or creating such other liability specifically provides to the contrary.

12.9 Acknowledgement and Consent to Bail-In of Affected Financial Institutions. Notwithstanding anything to the contrary in any Loan Document or in any other agreement, arrangement or understanding among any such parties, each party hereto acknowledges that any liability of any Affected Financial Institution arising under any Loan Document, to the extent such liability is unsecured, may be subject to the write-down and conversion powers of the applicable Resolution Authority and agrees and consents to, and acknowledges and agrees to be bound by:

(a) the application of any Write-Down and Conversion Powers by the applicable Resolution Authority to any such liabilities arising hereunder that may be payable to it by any party hereto that is an Affected Financial Institution; and

(b) the effects of any Bail-in Action on any such liability, including, if applicable:

(i) a reduction in full or in part or cancellation of any such liability;

(ii) a conversion of all, or a portion of, such liability into shares or other instruments of ownership in such affected Financial Institution, its parent undertaking, or a bridge institution that may be issued to it or otherwise conferred on it, and that such shares or other instruments of ownership will be accepted by it in lieu of any rights with respect to any such liability under this Agreement or any other Loan Document; or

(iii) the variation of the terms of such liability in connection with the exercise of the write-down and conversion powers of the applicable Resolution Authority.

12.10 Acknowledgement Regarding Any Supported QFCs. To the extent that the Loan Documents provide support, through a guarantee or otherwise, for Hedge Agreements or any other agreement or instrument that is a QFC (such support, "QFC Credit Support" and each such QFC a "Supported QFC"), the parties acknowledge and agree as follows with respect to the resolution power of the Federal Deposit Insurance Corporation under the Federal Deposit Insurance Act and Title II of the Dodd-Frank Wall Street Reform and Consumer Protection Act (together with the regulations promulgated thereunder, the "U.S. Special Resolution Regimes") in respect of such Supported QFC and QFC Credit Support (with the provisions below applicable notwithstanding that the Loan Documents and any Supported QFC may in fact be stated to be governed by the laws of the State of New York and/or of the United States or any other state of the United States):

In the event a Covered Entity that is party to a Supported QFC (each, a "Covered Party") becomes subject to a proceeding under a U.S. Special Resolution Regime, the transfer of such Supported QFC and the benefit of such QFC Credit Support (and any interest and obligation in or under such Supported QFC and such QFC Credit Support, and any rights in property securing such Supported QFC or such QFC Credit Support) from such Covered Party will be effective to the same extent as the transfer would be effective under the U.S. Special Resolution Regime if the Supported QFC and such QFC Credit Support (and any such interest, obligation and rights in property) were governed by the laws of the United States or a state of the United States. In the event a Covered Party or a BHC Act Affiliate of a Covered Party becomes subject to a proceeding under a U.S. Special Resolution Regime, Default Rights under the Loan Documents that might otherwise apply to such Supported QFC or any QFC Credit Support that may be exercised against such Covered Party are permitted to be exercised to no greater extent than such Default Rights could be exercised under the U.S. Special Resolution Regime if the Supported QFC and the Loan Documents were governed by the laws of the United States or a state of the United States. Without limitation of the foregoing, it is understood and agreed that rights and remedies of the parties with respect to a Defaulting Lender shall in no event affect the rights of any Covered Party with respect to a Supported QFC or any QFC Credit Support.

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Exhibit B

SCHEDULE 1.1

COMMITMENTS

[***]

List of Subsidiaries

Entity Name	Place of Incorporation	Ownership % as of December 31, 2022
BB Square Capital Investors I, LP	Delaware	100.0%
BB Square Capital, LLC	Delaware	100.0%
BB Square Holdings, LLC	Delaware	100.0%
BB Square Investors GP I, LLC	Delaware	100.0%
BB Square LP Investment, LLC	Delaware	100.0%
BridgeBio Chemistry, Inc.	Delaware	100.0%
BridgeBio Gene Therapy LLC	Delaware	100.0%
BridgeBio Gene Therapy Research, Inc.	Delaware	100.0%
BridgeBio Pharma LLC	Delaware	100.0%
BridgeBio Services Inc.	Delaware	100.0%
Calcilytix Therapeutics, Inc.	Delaware	100.0%
Cyan Therapeutics, Inc.	Delaware	100.0%
DTD Therapeutics, Inc.	Delaware	100.0%
Eidos Therapeutics, Inc.	Delaware	100.0%
Sub20, Inc.	Delaware	100.0%
CoA Therapeutics, Inc.	Delaware	100.0%
Origin Biosciences, Inc.	Delaware	99.9%
TheRas, Inc.	Delaware	99.9%
Portal Therapeutics, Inc.	Delaware	99.6%
Adrenas Therapeutics, Inc.	Delaware	99.1%
QED Therapeutics, Inc.	Delaware	99.0%
Sub22, Inc.	Delaware	98.5%
Ferro Therapeutics, Inc.	Delaware	98.2%
Eulamin Therapeutics, Inc.	Delaware	98.0%
Sub21, Inc.	Delaware	98.0%
Aspa Therapeutics, Inc.	Delaware	98.0%
Cantero Therapeutics, Inc.	Delaware	96.5%
Venthera, Inc.	Delaware	96.1%
G Protein Therapeutics, Inc.	Delaware	95.2%
Molecular Skin Therapeutics, Inc.	Delaware	91.4%
Phoenix Tissue Repair, Inc.	Delaware	85.8%
Navire Pharma, Inc.	Delaware	80.8%
ML Bio Solutions, Inc.	Delaware	76.1%
Sen Therapeutics, Inc.	Delaware	64.4%
PellePharm, Inc.	Delaware	43.2%
Audition Therapeutics, Inc.	Delaware	34.4%
BridgeBio Pharma Canada, ULC	Canada	100.0%
BridgeBio Pharma Cayman	Cayman Islands	100.0%
BridgeBio France SAS	France	100.0%
BridgeBio Germany, GmbH	Germany	100.0%
BridgeBio Pharma (HK) Limited	Hong Kong	100.0%
BridgeBio Europe B.V.	Netherlands	100.0%
BridgeBio International GmbH	Switzerland	100.0%
BridgeBio UK Limited	United Kingdom	100.0%

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in the following Registration Statements:

• Registration Statement No. 333-269600 and 333-263009 on Form S-8 pertaining to the 2021 Amended and Restated Stock Option and Incentive Plan
• Registration Statement No. 333-232491 and 333-236872 on Form S-8 pertaining to the 2019 Stock Option and Incentive Plan and 2019 Employee Stock Purchase Plan
• Registration Statement No. 333-234803 on Form S-8 pertaining to the 2019 Inducement Equity Plan
• Registration Statement No. 333-239718 on Form S-8 pertaining to the Amended and Restated 2019 Stock Option and Incentive Plan
• Registration Statement No. 333-252393 on Form S-8 pertaining to the Eidos Therapeutics, Inc. Amended and Restated 2018 Stock Option and Incentive Plan and Eidos Therapeutics, Inc. Amended and Restated 2016 Equity Incentive Plan
• Registration Statement No. 333-252394 on Form S-8 pertaining to the Amended and Restated 2019 Stock Option and Incentive Plan and Amended and Restated 2019 Employee Stock Purchase Plan
• Registration Statement No. 333-239734 and 333-240147 on Form S-3ASR

of our reports dated February 23, 2023, relating to the consolidated financial statements of BridgeBio Pharma, Inc. and the effectiveness of BridgeBio Pharma, Inc.'s internal control over financial reporting appearing in this Annual Report on Form 10-K for the year ended December 31, 2022.

/s/ Deloitte & Touche LLP

San Francisco, California
February 23, 2023

Exhibit 31.1

CERTIFICATIONS

I, Neil Kumar, certify that:

1. I have reviewed this Annual Report of BridgeBio Pharma, Inc. on Form 10-K for the period ended December 31, 2022 as filed with the Securities and Exchange Commission on the date hereof (the "Report");

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

February 23, 2023

/s/ Neil Kumar

Neil Kumar
Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATIONS

I, Brian Stephenson, certify that:

1. I have reviewed this Annual Report of BridgeBio Pharma, Inc. on Form 10-K for the period ended December 31, 2022 as filed with the Securities and Exchange Commission on the date hereof (the "Report");

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

February 23, 2023

/s/ Brian Stephenson

Brian Stephenson
Chief Financial Officer
(Principal Financial and Accounting Officer)

Exhibit 32.1

**CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO SECTION 906
OF THE SARBANES-OXLEY ACT OF 2002**

In connection with the Annual Report of BridgeBio Pharma, Inc. (the “Company”) on Form 10-K for the period ended December 31, 2022 as filed with the Securities and Exchange Commission on the date hereof (the “Report”), I, Neil Kumar, the Chief Executive Officer of BridgeBio Pharma, Inc. (the “Company”), do hereby certify in accordance with 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002 that, based upon my knowledge:

1. This Annual Report on Form 10-K of the Company, to which this certification is attached as an exhibit (the “Report”), fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and
2. The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

February 23, 2023

/s/ Neil Kumar

Neil Kumar
Chief Executive Officer
(Principal Executive Officer)

A signed original of this written statement required by Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended, and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. Section 1350), has been provided to BridgeBio Pharma, Inc. and will be retained by BridgeBio Pharma, Inc. and furnished to the Securities and Exchange Commission or its staff upon request. This certification accompanies the Form 10-K to which it relates, is not deemed filed with the Securities and Exchange Commission and is not to be incorporated by reference into any filing of BridgeBio Pharma, Inc. under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended (whether made before or after the date of the Form 10-K), irrespective of any general incorporation language contained in such filing.

Exhibit 32.2

**CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO SECTION 906
OF THE SARBANES-OXLEY ACT OF 2002**

In connection with the Annual Report of BridgeBio Pharma, Inc. (the “Company”) on Form 10-K for the period ended December 31, 2022 as filed with the Securities and Exchange Commission on the date hereof (the “Report”), I, Brian Stephenson, Chief Financial Officer (Principal Financial and Accounting Officer) of the Company, certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that:

1. The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and
2. Information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

February 23, 2023	/s/ Brian Stephenson
	Brian Stephenson *Chief Financial Officer* *(Principal Financial and Accounting Officer)*

A signed original of this written statement required by Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended, and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. Section 1350), has been provided to BridgeBio Pharma, Inc. and will be retained by BridgeBio Pharma, Inc. and furnished to the Securities and Exchange Commission or its staff upon request. This certification accompanies the Form 10-K to which it relates, is not deemed filed with the Securities and Exchange Commission and is not to be incorporated by reference into any filing of BridgeBio Pharma, Inc. under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended (whether made before or after the date of the Form 10-K), irrespective of any general incorporation language contained in such filing.