PRECISION
BIOSCIENCES

Fiscal Year

2020 Annual Report

Dedicated to
IMPROVING
LIFE

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, 2020
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 Number 001-38841

Precision BioSciences, Inc.
(Exact name of registrant as specified in its charter)

Delaware	**20-4206017**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
302 East Pettigrew St., Suite A-100 Durham, North Carolina	**27701**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: (919) 314-5512

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 $0.000005 per share	DTIL	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 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. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. YES ☐ NO ☒

Indicate by check mark whether the Registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). YES ☐ NO ☒

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the Registrant, based on the closing price of the shares of common stock on The Nasdaq Global Select Market on June 30, 2020, was $382.8 million.

The number of shares of Registrant's common stock outstanding as of March 2, 2021 was 56,986,188.

DOCUMENTS INCORPORATED BY REFERENCE

None.

Table of Contents

		Page
PART I		
Item 1.	Business	1
Item 1A.	Risk Factors	46
Item 1B.	Unresolved Staff Comments	97
Item 2.	Properties	97
Item 3.	Legal Proceedings	97
Item 4.	Mine Safety Disclosures	97
PART II		
Item 5.	Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities	98
Item 6.	Selected Financial Data	98
Item 7.	Management's Discussion and Analysis of Financial Condition and Results of Operations	99
Item 7A.	Quantitative and Qualitative Disclosures About Market Risk	115
Item 8.	Financial Statements and Supplementary Data	116
Item 9.	Changes in and Disagreements with Accountants on Accounting and Financial Disclosure	116
Item 9A.	Controls and Procedures	116
Item 9B.	Other Information	116
PART III		
Item 10.	Directors, Executive Officers and Corporate Governance	117
Item 11.	Executive Compensation	117
Item 12.	Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters	117
Item 13.	Certain Relationships and Related Transactions, and Director Independence	117
Item 14.	Principal Accounting Fees and Services	117
PART IV		
Item 15.	Exhibits, Financial Statement Schedules	118
Item 16	Form 10-K Summary	121

[THIS PAGE INTENTIONALLY LEFT BLANK]

FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. We intend such forward-looking statements to be covered by the safe harbor provisions for forward-looking statements contained in Section 27A of the Securities Act of 1933, as amended (the "Securities Act") and Section 21E of the Securities Exchange Act of 1934, as amended (the "Exchange Act"). All statements other than statements of present and historical facts contained in this Annual Report on Form 10-K, including without limitation, statements regarding our future results of operations and financial position, business strategy and approach, including related results, prospective products, planned preclinical or greenhouse studies and clinical or field trials, the status and results of our preclinical and clinical studies, expected release of interim data, expectations regarding our allogeneic chimeric antigen receptor T cell immunotherapy product candidates, expectations regarding the use and effects of ARCUS, including in connection with *in vivo* genome editing, potential new partnerships or alternative opportunities for our product candidates, capabilities of our manufacturing facility, regulatory approvals, research and development costs, timing, expected results and likelihood of success, plans and objectives of management for future operations, as well as the impact of the COVID-19 pandemic may be forward-looking statements. Without limiting the foregoing, in some cases, you can identify forward-looking statements by terms such as "aim," "may," "will," "should," "expect," "exploring," "plan," "anticipate," "could," "intend," "target," "project," "contemplate," "believe," "estimate," "predict," "potential," "seeks," or "continue" or the negative of these terms or other similar expressions, although not all forward-looking statements contain these words. No forward-looking statement is a guarantee of future results, performance, or achievements, and one should avoid placing undue reliance on such statements.

Forward-looking statements are based on our management's beliefs and assumptions and on information currently available to us. Such beliefs and assumptions may or may not prove to be correct. Additionally, such forward-looking statements are subject to a number of known and unknown risks, uncertainties and assumptions, and actual results may differ materially from those expressed or implied in the forward-looking statements due to various factors, including, but not limited to, those identified in Part I. Item 1A. "Risk Factors" and Part II. Item 7. "Management's Discussion and Analysis of Financial Condition and Results of Operations." These risks and uncertainties include, but are not limited to:

- our ability to become profitable;
- our ability to procure sufficient funding and requirements under our current debt instruments and effects of restrictions thereunder;
- risks associated with raising additional capital;
- our operating expenses and our ability to predict what those expenses will be;
- our limited operating history;
- the success of our programs and product candidates in which we expend our resources;
- our dependence on our ARCUS technology;
- the risk that other genome-editing technologies may provide significant advantages over our ARCUS technology;
- the initiation, cost, timing, progress, achievement of milestones and results of research and development activities, preclinical or greenhouse studies and clinical or field trials;
- public perception about genome editing technology and its applications;
- competition in the genome editing, biopharmaceutical, biotechnology and agricultural biotechnology fields;
- our or our collaborators' ability to identify, develop and commercialize product candidates;
- pending and potential liability lawsuits and penalties against us or our collaborators related to our technology and our product candidates;
- the U.S. and foreign regulatory landscape applicable to our and our collaborators' development of product candidates;
- our or our collaborators' ability to obtain and maintain regulatory approval of our product candidates, and any related restrictions, limitations and/or warnings in the label of an approved product candidate;
- our or our collaborators' ability to advance product candidates into, and successfully design, implement and complete, clinical or field trials;
- potential manufacturing problems associated with the development or commercialization of any of our product candidates;
- our ability to obtain an adequate supply of T cells from qualified donors;

- our ability to achieve our anticipated operating efficiencies at our manufacturing facility;
- delays or difficulties in our and our collaborators' ability to enroll patients;
- changes in interim "top-line" data that we announce or publish;
- if our product candidates do not work as intended or cause undesirable side effects;
- risks associated with applicable healthcare, data privacy and security regulations and our compliance therewith;
- the rate and degree of market acceptance of any of our product candidates;
- the success of our existing collaboration agreements, and our ability to enter into new collaboration arrangements;
- our current and future relationships with third parties including suppliers and manufacturers;
- our ability to obtain and maintain intellectual property protection for our technology and any of our product candidates;
- potential litigation relating to infringement or misappropriation of intellectual property rights;
- our ability to effectively manage the growth of our operations;
- our ability to attract, retain, and motivate key scientific and management personnel;
- market and economic conditions;
- effects of system failures and security breaches;
- effects of natural and manmade disasters, public health emergencies and other natural catastrophic events;
- effects of COVID-19, or any pandemic, epidemic, or outbreak of an infectious disease;
- insurance expenses and exposure to uninsured liabilities;
- effects of tax rules; and
- risks related to ownership of our common stock, including fluctuations in our stock price.

Moreover, we operate in an evolving environment. New risk factors and uncertainties may emerge from time to time, and it is not possible for management to predict all risk factors and uncertainties.

You should read this Annual Report on Form 10-K and the documents that we reference herein completely and with the understanding that our actual future results may be materially different from what we expect. We qualify all of our forward-looking statements by these cautionary statements. All forward-looking statements contained herein speak only as of the date of this Annual Report on Form 10-K. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise.

As used in this Annual Report on Form 10-K, unless otherwise stated or the context requires otherwise, references to "Precision," the "Company," "we," "us," and "our," refer to Precision BioSciences, Inc. and its subsidiaries on a consolidated basis.

RISK FACTOR SUMMARY

Our business is subject to numerous risks and uncertainties, including those described in Part I. Item 1A. "Risk Factors" in this Annual Report on Form 10-K. You should carefully consider these risks and uncertainties when investing in our common stock. Some of the principal risks and uncertainties include the following.

- *We have incurred significant operating losses since our inception and expect to continue to incur losses for the foreseeable future. We have never been profitable, and may never achieve or maintain profitability.*

- *We will need substantial additional funding, and if we are unable to raise a sufficient amount of capital when needed on acceptable terms, or at all, we may be forced to delay, reduce or eliminate some or all of our research programs, product development activities and commercialization efforts.*

- *We have a limited operating history, which makes it difficult to evaluate our current business and future prospects and may increase the risk of your investment.*

- *ARCUS is a novel technology, making it difficult to predict the time, cost and potential success of product candidate development. We have not yet been able to assess the safety and efficacy of most of our product candidates in humans, and have only limited safety and efficacy information in humans to date regarding one of our product candidates.*

- *We are heavily dependent on the successful development and translation of ARCUS, and due to the early stages of our product development operations, we cannot give any assurance that any product candidates will be successfully developed and commercialized.*

- *Adverse public perception of genome editing may negatively impact the developmental progress or commercial success of products that we develop alone or with collaborators.*

- *We face significant competition in industries experiencing rapid technological change, and there is a possibility that our competitors may achieve regulatory approval before us or develop product candidates or treatments that are safer or more effective than ours, which may harm our financial condition and our ability to successfully market or commercialize any of our product candidates.*

- *Our future profitability, if any, depends in part on our and our collaborators' ability to penetrate global markets, where we would be subject to additional regulatory burdens and other risks and uncertainties associated with international operations that could materially adversely affect our business.*

- *Product liability lawsuits against us could cause us to incur substantial liabilities and could limit commercialization of any products that we develop alone or with collaborators.*

- *The regulatory landscape that will apply to development of therapeutic product candidates by us or our collaborators is rigorous, complex, uncertain and subject to change, which could result in delays or termination of development of such product candidates or unexpected costs in obtaining regulatory approvals.*

- *Clinical trials are difficult to design and implement, expensive, time-consuming and involve an uncertain outcome, and the inability to successfully and timely conduct clinical trials and obtain regulatory approval for our product candidates would substantially harm our business.*

- *Even if we obtain regulatory approval for any products that we develop alone or with collaborators, such products will remain subject to ongoing regulatory requirements, which may result in significant additional expense.*

- *Even if any product we develop alone or with collaborators receives marketing approval, such product 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 ongoing novel coronavirus disease, COVID-19 has impacted our business and any other pandemic, epidemic or outbreak of an infectious disease may materially and adversely impact our business, including our preclinical studies and clinical trials.*

PART I

Item 1. Business.

We are a life sciences company dedicated to improving life through the application of our pioneering, proprietary ARCUS genome editing platform. We leverage ARCUS in the development of our product candidates, which are designed to treat human diseases and create healthy and sustainable food and agricultural solutions. We are actively developing product candidates in three innovative areas: allogeneic CAR T cell immunotherapy, *in vivo* gene correction, and food. We are currently conducting a Phase 1/2a clinical trial of PBCAR0191 in adult patients with relapsed or refractory, or R/R, non-Hodgkin lymphoma, or NHL, or R/R B-cell precursor acute lymphoblastic leukemia, or B-ALL. PBCAR0191 is our first gene-edited allogeneic chimeric antigen receptor, or CAR, T cell therapy candidate targeting CD19 and is being developed in collaboration with Les Laboratoires Servier, or Servier, pursuant to a development and commercial license agreement, as amended (the "Servier Agreement"). We have received orphan drug designation, for PBCAR0191 from the U.S. Food and Drug Administration ("FDA"), for the treatment of acute lymphoblastic leukemia, or ALL. In August 2020, the FDA granted Fast Track Designation for PBCAR0191 for the treatment of B-ALL. The NHL cohort will include patients with mantle cell lymphoma ("MCL"), an aggressive subtype of NHL, for which we have received orphan drug designation from the FDA. Made from donor-derived T cells modified using our ARCUS genome editing technology, PBCAR0191 recognizes the well characterized tumor cell surface protein CD19, an important and validated target in several B-cell cancers, and is designed to avoid graft-versus-host disease, or GvHD, a significant complication associated with donor-derived, cell-based therapies. We believe that this trial, which is designed to assess the safety and tolerability of PBCAR0191 at increasing dose levels, as well as to evaluate anti-tumor activity, is the first U.S.-based clinical trial to evaluate an allogeneic CAR T therapy for R/R NHL. Furthermore, we believe that our proprietary, one-step engineering process for producing allogeneic CAR T cells with a potentially optimized cell phenotype, at large scale in a cost-effective manner, will enable us to overcome the fundamental clinical and manufacturing challenges that have limited the CAR T field to date. We expect to report updated interim data for the PBCAR0191 study in mid-year 2021.

In April 2020, we commenced patient dosing in a Phase 1/2a clinical trial with our second allogeneic CAR T cell therapy product candidate, PBCAR20A. PBCAR20A is wholly owned by us and targets the validated tumor cell surface target CD20. It is being investigated in R/R NHL, including those with R/R chronic lymphocytic leukemia, CLL, or R/R small lymphocytic lymphoma, or SLL. A subset of the NHL patients will have the diagnosis of MCL and we have received orphan drug designation for PBCAR20A from the FDA for the treatment of this disease. Based on the safety profile observed to date with PBCAR0191, the FDA allowed us to commence dosing with PBCAR20A directly at 1×10^6 cells/kg. The study has continued to escalate through dose level two (3×10^6 cells/kg), and, in February 2021, we commenced patient dosing at dose level 3 (480×10^6 cell fixed dose) with a max dose of 6×10^6 cells/kg. We expect to report interim data for the PBCAR20A study in 2021.

In June 2020, we commenced patient dosing in a Phase 1/2a clinical trial with our third allogenic CAR T cell therapy product candidate, PBCAR269A. The starting dose of PBCAR269A is 6×10^5 cells/kg. PBCAR269A is wholly owned by us and is designed to target the validated tumor cell surface target BCMA. It is being investigated in subjects with R/R multiple myeloma and we have received orphan drug designation and Fast Track Designation from the FDA for this indication. In September 2020, we announced that we entered into a clinical trial collaboration with SpringWorks Therapeutics, Inc. ("SpringWorks"), a clinical-stage biopharmaceutical company focused on developing medicines for patients with severe rare diseases and cancer. Pursuant to the collaboration, PBCAR269A will be evaluated in combination with nirogacestat, SpringWorks' investigational gamma secretase inhibitor ("GSI"), in patients with R/R multiple myeloma, which is expected to commence in the first half of 2021. In February 2021, we commenced patient dosing at the highest dose cohort, dose level 3 of 6×10^6 cells/kg and we expect to report interim data on the PBCAR269A trial in 2021.

Additionally, in June 2020, Elo Life Systems ("Elo"), our wholly-owned subsidiary, established a strategic partnership with the Dole Food Company ("Dole") and entered into a Research, Development, and Commercialization Agreement with Dole, with the aim to co-develop banana varieties resistant to Fusarium oxysporum f. sp cubense Tropical race 4 ("Foc TR4"), utilizing proprietary computational biology workflows and the ARCUS genome editing platform. The disease caused by Foc TR4, commonly known as Fusarium wilt, threatens the continued cultivation of the world's most popular variety of banana called Cavendish, which is of considerable economic significance as this variety is used to produce export bananas for key markets around the globe and Dole is one of the largest producers in the industry. Fungicides, or other traditional means of disease control have failed as the pandemic continues to spread across vital banana growing economies.

In September 2020, we regained full clinical development and commercialization rights, and all data we generated for the *in vivo* chronic hepatitis B virus ("HBV") program developed under our 2018 collaboration agreement with Gilead Sciences. We are exploring partnership or alternative opportunities to enable the continued development of ARCUS-based HBV therapies.

In October 2020, we announced the U.S. Patent and Trademark Office's Patent Trial and Appeal Board ("PTAB") issued judgements in our favor in two patent interference proceedings that challenged nine U.S. patents we owned. The patents, which issued in 2018, relate to allogeneic CAR T cells produced by inserting a gene encoding a CAR into the T cell receptor ("TCR") alpha chain ("TRAC")

locus, as well as methods of using those cells for cancer immunotherapy. In the interference proceedings, a third party argued that it had invented the technology in 2012. The PTAB, however, found that the third-party patent application did not satisfy the written description requirement and rejected these claims while maintaining the claims in all nine of our patents.

In November 2020, we announced a research collaboration and exclusive license agreement with Eli Lilly and Company ("Lilly") to utilize ARCUS for the research and development of potential *in vivo* therapies for genetic disorders, with an initial focus on Duchenne muscular dystrophy ("DMD") and two other undisclosed gene targets. Under the agreement, Lilly has the right to nominate up to three additional gene targets for genetic disorders over the first four years of the Development and License Agreement, which may be extended to six years upon Lilly's election and payment of an extension fee.

In December 2020, we announced interim clinical results from our Phase 1/2a study of PBCAR0191 as a treatment of R/R NHL and R/R B-ALL. As of the November 16, 2020 cutoff, 27 patients including 16 patients with aggressive NHL and 11 patients with aggressive B-ALL were enrolled and evaluated. In this dose escalation and dose expansion study, PBCAR0191 had an acceptable safety profile with no cases of graft versus host disease, no cases of Grade ≥ 3 cytokine release syndrome, and no cases of Grade ≥ 3 neurotoxicity. PBCAR0191 demonstrated longest durability of response to 11 months in B-ALL. PBCAR0191 with enhanced lymphodepletion ("eLD") resulted in objective response rate of 83% (5/6) in NHL and B-ALL as compared to 33% (3/9) in NHL with standard lymphodepletion ("sLD").

Additionally, in December 2020, researchers at Elo in collaboration with Alan Chambers, Ph.D., and the Tropical Research and Education Center at the University of Florida published a paper in *Nature Food*, reporting a chromosome-scale, phased *Vanilla planifolia* genome, which revealed sequence variants for genes that may impact the vanillin pathway, and therefore influence bean quality, including its productivity, flower anatomy, and disease resistance.

In January 2021, we announced that the FDA has accepted our Initial New Drug ("IND") application for PBCAR19B, our next-generation, stealth cell, CD19 allogenic CAR T candidate for Non-Hodgkin Lymphoma, and we expect to begin the Phase 1 study by mid-2021. Additionally, in January 2021, we announced that we received a Notice of Allowance from the U.S. Patent and Trademark Office for a patent application covering PBCAR19B. The allowed composition claims of this patent application encompass genetically-modified human T cells comprising the PBCAR19B construct, which is inserted within the T cell receptor alpha constant locus. Once issued, patents arising from this patent family will have standard expiration dates in April 2040. In preclinical studies, PBCAR19B has shown to delay both T cell and natural killer cell mediated allogeneic rejection in vitro and may improve the persistence of allogeneic CAR T cells.

We expect to advance a program targeting the rare genetic disease primary hyperoxaluria type 1 ("PH1") as our lead wholly owned *in vivo* gene correction program. PH1 affects approximately 1-3 people per million in the United States and is caused by loss of function mutations in the AGXT gene, leading to the accumulation of calcium oxalate crystals in the kidneys. Patients suffer from painful kidney stones which may ultimately lead to renal failure. Using ARCUS, we are developing a potential therapeutic approach to PH1 that involves knocking out a gene called HAO1 which acts upstream of AGXT. Suppressing HAO1 has been shown in preclinical models by us to prevent the formation of calcium oxalate. We therefore believe that a one-time administration of an ARCUS nuclease targeting HAO1 may be a viable strategy for a durable treatment of PH1 patients. Pre-clinical research has continued to progress, and we expect to provide an update on this program in the first half of 2021.

In January 2021, we disclosed our intention to spinout our wholly owned subsidiary, Elo. We are continuing to explore our strategic options, and the timing of any such sale, spinout or other treatment of Elo remains uncertain.

Our Pipeline

Allogeneic CAR T Immunotherapy

We believe that we have developed a transformative allogeneic CAR T immunotherapy platform with the potential to overcome certain limitations of autologous CAR T cell therapies and significantly increase patient access to these cutting-edge treatments. Cancer immunotherapy is a type of cancer treatment that uses the body's immune system to fight the disease. CAR T is a form of immunotherapy in which a specific type of immune cell, called a "T cell", is genetically engineered to recognize and kill cancer cells. Current commercially available CAR T therapies are autologous, meaning the T cells used as the starting material for this engineering process are derived directly from the patient. As a consequence, the therapy is highly personalized, difficult to scale, and expensive. Our allogeneic approach uses donor-derived T cells that are gene edited using ARCUS and are designed for safe delivery to an unrelated patient. We believe that this donor-derived approach will allow us to consistently produce a potent product by selecting donors with high quality T cells and will lessen the product-to-product variability seen in autologous therapies. We are able to produce allogeneic CAR T cells at a large scale in a cost-effective manner and have the potential to overcome the "one patient: one product" burden of autologous CAR T cell therapies.

Leveraging the unique gene editing capabilities of ARCUS, we have developed a one-step cell engineering process for allogeneic CAR T cells that is designed to maintain naïve and central memory T cell phenotypes throughout the CAR T manufacturing process, which we believe to be important for an optimized CAR T therapy. Due to our one-step editing method and the decision early in the development of our allogeneic CAR T immunotherapy platform to invest in process development, we have scaled our manufacturing process and are currently producing allogeneic CAR T cells at large scale in accordance with current good manufacturing practice, or cGMP.

In February 2016, we entered into the Servier Agreement. Pursuant to this agreement we have agreed to perform early-stage research and development on individual T cell modifications for five unique antigen targets. Servier selected one target at the Servier Agreement's inception and, during 2020, selected two additional hematological cancer targets beyond CD19 and two new solid tumor targets. With the addition of these new targets, we received development milestone payments in 2020 and may be eligible to receive additional development milestone payments in 2021. Upon selection of an antigen target, we have agreed to develop the resulting therapeutic product candidates through Phase 1 clinical trials and prepare the clinical supply of such product candidates for use in Phase 2 clinical trials. We have the ability to opt-in to a 50/50 co-development and co-promotion agreement in the United States on all licensed products under the Servier Agreement.

Our most advanced program, PBCAR0191, is an allogeneic CAR T cell therapy candidate targeting the well-validated tumor target CD19 and is being developed for the treatment of adult patients with NHL and B-ALL. CD19 is a protein that is expressed on the surface of B cells. The FDA has granted PBCAR0191 orphan drug designation for the treatment of ALL and, in August 2020 granted PBCAR0191 Fast Track Designation for treatment of B-ALL.

We reported updated interim data from our ongoing Phase 1/2a clinical trial of PBCAR0191 including response rates across R/R NHL and R/R B-ALL patient cohorts as further described in "Our Allogeneic CAR T Immunotherapy Pipeline."

PBCAR0191, which incorporates our patented N6 co-stimulatory domain, demonstrated a clear dose dependent increase in peak cell expansion. Compared to sLD, eLD with PBCAR0191 at DL3 resulted in approximately 95-fold increase in peak cell expansion, and approximately 45-fold increase in area under the curve. This was associated with a higher CR rate in NHL (75%).

In this dose escalation and dose expansion study, PBCAR0191 had an acceptable safety profile with no cases of graft versus host disease, no cases of Grade ≥ 3 cytokine release syndrome, and no cases of Grade ≥ 3 immune effector cell neurotoxicity.

One NHL patient who was treated with PBCAR0191 and eLD had previously received nine prior lines of therapy before entering the trial. The patient presented with persistent cytopenias at baseline and a history of infections, including bacterial sepsis. The patient had an episode of sepsis at day 27 which appeared to have resolved at day 33, following which a partial response was achieved at day 34. Unfortunately, the patient died at day 42 with grade 5 sepsis. We reported the serious adverse event to the FDA and reported the patient death.

We are enrolling additional patients with eLD and plan to present updated interim data on this study by mid-2021.

***In vivo* Gene Correction.** Our goal is to cure genetic diseases by correcting the DNA errors responsible for causing them. *In vivo* gene corrections are gene corrections that take place in a living organism. We have advanced a deep portfolio of diverse programs toward preclinical efficacy and toxicity studies. We have generated a significant large animal dataset that we believe to be the most comprehensive of any in the field and have observed high-efficiency *in vivo* genome editing in non-human primates ("NHPs") in our preclinical studies, as highlighted in our July 2018 publication in *Nature Biotechnology*. We believe this is the first peer-reviewed publication of *in vivo* genome editing data in NHPs. In our preclinical studies, we observed the high-efficiency editing of the PCSK9 gene in NHPs using ARCUS and, even at the highest dose, the treatment was observed to be well-tolerated. As published in *Molecular Therapy* in February 2021, the NHPs have been monitored for more than three years and have continued to show a sustained reduction in low density lipoprotein cholesterol levels while maintaining stable gene editing without any obvious adverse effects. After the one-time vector administration more than three years ago, NHPs treated with ARCUS have experienced stable reductions of up to 85% in PCSK9 protein levels and a 56% reduction of low-density lipoprotein ("LDL") cholesterol levels.

We expect to advance a program for the treatment of the rare genetic disease PH1 as our lead wholly owned gene correction program, based on preclinical data we have generated high efficiency knock out of the HAO1 target gene in NHPs using ARCUS, and evidence from a mouse model of clinically meaningful biomarker changes using our approach. We expect to provide an update on this program during the first half of 2021.

As discussed above, in November 2020, we announced a research collaboration and exclusive license agreement with Lilly, pursuant to which we will be responsible for conducting certain pre-clinical research and IND-enabling activities with respect to the gene targets nominated by Lilly. Lilly will be responsible for conducting clinical development and commercialization activities for licensed products resulting from the collaboration and may engage with us for additional clinical and/or initial commercial manufacture of licensed products.

We expect to advance a program for the treatment of the rare genetic disease PH1 as our lead wholly owned gene correction program, based on preclinical data we have generated high efficiency knock out of the HAO1 target gene in NHPs using ARCUS, and evidence from a mouse model of clinically meaningful biomarker changes using our approach. We expect to provide an update on this program during the first half of 2021.

We are also in the discovery stage for other *in vivo* indications: lipoprotein lipase deficiency, familial amyloid polyneuropathy, familial hypercholesterolemia, and autosomal dominant retinitis pigmentosa.

Food. Our food platform, which we operate through our wholly owned subsidiary, Elo, is an integrated suite of gene discovery and crop engineering technologies that is designed to generate products in collaboration with leading food producers. Elo has a team with in-depth experience in crop genome editing. Over the last decade, Elo has worked with some of the largest plant biotechnology companies to edit gene targets and develop potential product candidates in a variety of crop plants. By combining the power of the ARCUS technology platform with target discovery, transformation and high throughput trait evaluation, Elo has enabling our partners to potentially address critical issues in food and agriculture created by climate change and dramatic shifts in consumer preference toward healthier eating. Elo's collaboration-driven business model enables Elo to remain capital efficient throughout the product development cycle while generating revenue through various revenue-sharing models. Elo achieved proof of concept with its ZeroMelon™ watermelon-based sweetener program and advanced the program to greenhouse trials. This program is intended to leverage ARCUS to develop a scalable low-calorie sweetener. As discussed above, Elo also entered into a Research, Development, and Commercialization Agreement with Dole. with the aim to co-develop banana varieties resistant to FOC TR4, utilizing proprietary computational biology workflows and the ARCUS genome editing platform. Elo's ClimateSmart Chickpea program addresses the effect of climate change as a foundational trait for the plant-based protein industry. Edited chickpea plants were successfully created at a subsidiary of Elo in Australia in collaboration with the Queensland University of Technology. Genotypic and phenotypic screens are in progress.

Our Team

We believe that our team, whom we call Precisioneers, has among the deepest scientific experience and capabilities of all genome editing companies. Derek Jantz, Ph.D., our Chief Scientific Officer and a co-founder of Precision, and Jeff Smith, Ph.D., our Chief Technology Officer and also a co-founder of Precision, have been working with genome editing technology for more than 15 years. They are pioneers in the genome editing field and developed the ARCUS genome editing platform to address what they perceived as limitations in the existing genome editing technologies. Our Chief Executive Officer, Matthew Kane, also a co-founder of Precision, has almost 20 years' experience in life sciences, most of which has been working in genome editing.

We have selectively expanded our team of Precisioneers to include individuals with extensive industry experience and expertise in the discovery, development and manufacture of cell and gene therapies and the creation of innovative solutions to myriad problems affecting food systems. As of December 31, 2020, our team of Precisioneers included more than 57 scientists with Ph.D. degrees.

We are a purpose-driven organization, and we have carefully promoted a culture that values innovation, accountability, respect, adaptability and perseverance. We strive to ensure that our open, collaborative culture empowers Precisioneers to be their best selves and do their best work. We strongly believe that our shared values will help our team navigate and overcome challenges we may experience as we pursue our mission of improving life through genome editing. Our culture has helped build a world-class team with industry-leading experience in genome editing and continually attracts new talent to further build our capabilities. Our team is a group of motivated individuals that value the opportunity to contribute their time and talents toward the pursuit of improving life. Precisioneers appreciate high-quality research and are moved by the opportunity to translate their work into treatments and solutions that will impact human health.

Our Strategy

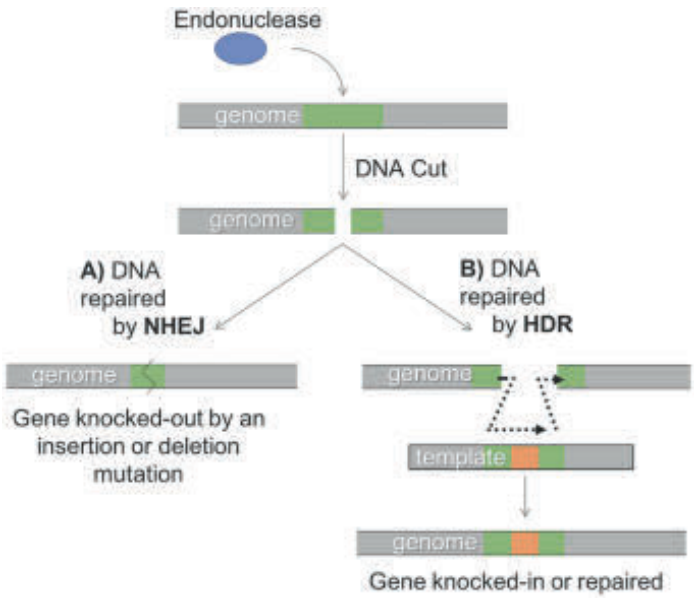
We are dedicated to improving life. Our goal is to broadly translate the potential of genome editing into permanent genetic solutions for significant unmet needs. Our strategy to achieve this goal includes the following key elements:

- **Create a fully integrated genome editing company capable of delivering solutions that address unmet needs impacting human health.** We believe that to be a leader in the field of genome editing and maximize the impact of our ARCUS genome editing platform, we must be able to control those elements of our business that may provide us with certain strategic advantages or operational efficiencies. We intend to continue to invest in comprehensive research, development, manufacturing and commercial capabilities that provide control and oversight of our product candidates from discovery through commercialization.
- **Capitalize on our emerging leadership position in allogeneic CAR T immunotherapies.** We believe that we have developed the first allogeneic CAR T cell platform capable of producing drug product at scale, with a potentially optimal cell profile for therapeutic efficacy and true off-the-shelf delivery without the need for harsh and potentially toxic lymphodepletion. We have selected three validated CAR T cell targets that we believe offer the greatest chance of clinical success for our initial product candidates. Our CAR T platform is modular, which we believe will allow us to leverage proof-of-concept from our ongoing and planned initial human trials for multiple other CAR T programs. We believe the combination of these factors, along with our unique ARCUS technology, puts us in a differentiated position to be the leader in the development of allogeneic CAR T therapies.
- **Advance ARCUS-based *in vivo* gene correction programs into human clinical trials.** In our preclinical studies, we observed the high-efficiency and tolerability of *in vivo* genome editing using ARCUS in a non-human primate model, as published in *Nature Biotechnology* in July 2018 and *Molecular Therapy* in February 2021. To our knowledge, we are the first company to complete this milestone, which we believe to be critical to successful *in vivo* genome editing therapeutic development. We have built on this early success by diligently advancing a diverse portfolio of preclinical *in vivo* gene correction programs through additional large animal studies, focusing initially on gene targets occurring in the liver and eye. As discussed above, in November 2020, we also announced a research collaboration and exclusive license agreement with Lilly to utilize ARCUS for the research and development of potential in vivo therapies for genetic disorders, with an initial focus on DMD and two other undisclosed gene targets.
- **Continue investing in the optimization of ARCUS and enabling technologies.** We believe that a key to our future success is the quality of the genome editing tools that we produce. Since our founding, we have devoted ourselves to continuously refining the precision and efficiency of our core genome editing platform. We intend to continue this investment in ARCUS while surrounding it with enabling technologies and expertise to retain what we believe is a leadership position in the field.
- **Create an environment that is a destination of choice for premier talent within the life sciences industry.** We believe that we currently have among the deepest and strongest skill set within the genome editing industry and credit much of our past success to our commitment to our team and culture. Our future success will depend on our ability to continue to attract and retain world-class talent within our markets of interest. We intend to consciously invest in fostering an environment within our company that is both challenging and supportive and inspires our team to broadly translate genome editing into permanent genetic solutions.
- **Expand the breadth of our operations through additional product platforms and strategic relationships.** We believe that the ARCUS genome editing platform has broad utility beyond our current areas of focus. We intend to invest in the development of additional product platforms and seek collaborations with companies with additive expertise in areas outside of our current target markets to maximize the value of our company.

Overview of Genome Editing

Deoxyribonucleic acid, or DNA, carries the genetic instructions for all basic functions of a living cell. These instructions are encoded in four different molecules, called bases, which are strung together in specific sequences to form genes. Each gene is responsible for a specific function in a cell, and the complete set of genes in a cell, which can consist of tens of thousands of genes and billions of individual bases, is known as a genome. The complete genome sequence has been determined for many organisms, including humans. This allows scientists to identify specific genes and determine how their unique sequences contribute to a particular cellular function. Studying variations in gene sequences further informs an understanding of why a cell behaves a certain way, which can greatly enhance understanding of what causes and how to treat aberrant behavior that leads to disease.

Genome editing is a biotechnology process that removes, inserts or repairs a portion of DNA at a specific location in a cell's genome. Early applications of genome editing focused on advancing genetic research. As genome editing technologies have advanced, their application is moving beyond understanding disease to treating or preventing disease by editing DNA. Genome editing is accomplished by delivering a DNA cutting enzyme, called an endonuclease, to a targeted segment of genetic code. Once the endonuclease cuts the DNA, the cell has to repair the break to survive and will generally do so in one of two ways, as shown below.



There are two primary mechanisms of DNA repair, non-homologous end joining, or NHEJ, and homology directed repair, or HDR. As shown in A) above, NHEJ is a pathway that repairs breaks in DNA without a template. NHEJ is the less precise method of repair that prioritizes speed over accuracy, making it prone to leaving insertions and/or deletions of DNA bases at the cut site. These insertions or deletions can disrupt the gene sequence and can be used to inactivate or "knock out" the function of the gene. Accordingly, genome editing technologies can be used to permanently knock out a gene in a cell or organism by creating a break in the DNA sequence of that gene.

As shown in B) above, HDR is a mechanism of DNA repair whereby the cell uses a second DNA molecule with a sequence similar to that of the cut DNA molecule to guide the repair process. Since HDR uses a "template" of similar genetic information to guide the repair process, it is the more precise mechanism of cellular repair. HDR results in the sequence of the template being copied permanently into the genome at the site of the DNA cut. If we provide a template DNA molecule directly to the edited cell and the cell repairs itself using HDR, a new gene can be incorporated or "knocked in" at a precise location in the genome. Alternatively, the use of HDR can "repair" a DNA mutation by correcting it to the proper functioning sequence when repairing the break. Thus, genome editing endonucleases can be used to introduce a variety of different changes to the genetic code of a cell or organism including gene knockout, gene insertion and gene repair.

There are several genome editing technologies, including ARCUS, zinc-finger nucleases, or ZFNs, TAL-effector nucleases, or TALENs, and CRISPR/Cas9. These technologies differ from one another principally in the properties of the endonuclease that they each employ. The different endonucleases have fundamentally different mechanisms of recognizing and cutting their DNA targets, which gives each technology advantages and disadvantages depending on how each is used.

Our Approach to Genome Editing

We are pioneers in the field of genome editing and have extensive experience with a breadth of genome editing technologies. Our ARCUS platform was developed to address limitations of other editing technologies that could impair their deployment for therapeutic applications. We looked to nature for examples of genome editing and found the I-CreI endonuclease from the algae *Chlamydomonas reinhardtii*. Unlike ZFN, TALEN or CRISPR/Cas9, I-CreI is a natural enzyme that evolved to edit a large, complex genome. In nature, it is responsible for modifying a specific location in the algae genome by inserting a gene using the HDR process, according to scientific literature.

We believe that I-CreI has a number of attributes that make it attractive for the development of novel genome editing endonucleases, such as:

- **Specificity.** Complex genome editing applications, especially those involving the human body, require a high level of endonuclease specificity to limit the likelihood that the endonuclease will recognize and edit any genetic sequence other than its intended target. Based on scientific literature, we believe that several attributes of I-CreI naturally inhibit off-target cutting. I-CreI.
- **Efficiency.** Most applications of genome editing technology require that a sufficient portion of the targeted cells are edited to achieve the desired result. The activity level of the endonuclease is one factor that can affect how many cells are edited. The slow catalytic mechanism of I-CreI imparts specificity but does not impact its on-target efficiency for genome editing purposes because genome editing involves cutting only a single site in a cell. As such, I-CreI is able to achieve a high level of on-target editing while rarely cutting off-target, as supported by scientific literature.
- **Delivery.** Size and structural simplicity affect the ease with which endonucleases can be delivered to cells for editing. I-CreI is very small relative to other genome editing endonucleases. It is approximately one quarter to one sixth of the size of the ZFN, TALEN and CRISPR/Cas9 endonucleases. Unlike those endonucleases, I-CreI can be delivered as a single gene. As such, we believe it is compatible with many different delivery mechanisms. Additionally, I-CreI's size and structure facilitate the simultaneous delivery of multiple engineered endonucleases to introduce more than one edit to a cell. Both of these properties significantly broaden the spectrum of potential applications for I-CreI-based genome editing endonucleases.
- **Type of Cut.** The three prime, or 3', overhangs created when I-CreI cuts DNA have been shown to promote DNA repair through a mechanism called "homology directed repair," or HDR. 3' overhangs are stretches of unpaired nucleotides in the end of a DNA molecule. A genome editing technology that facilitates cellular repair through HDR enables applications that require a gene insertion or gene repair. Unlike other editing endonucleases, I-CreI creates four base 3' overhangs when it cuts its DNA site, which increases the likelihood that the cell will repair the DNA cut through HDR. As such, the DNA cuts created by I-CreI can be exploited to efficiently insert or repair DNA, consistent with the natural role of I-CreI in catalyzing the targeted insertion of a gene in algae.
- **Programmability.** I-CreI recognizes its DNA target site through a complex network of interactions that is challenging to re-program for new editing applications involving different DNA sequences. The challenges associated with re-programming I-CreI have, historically, hampered its adoption by the genome editing community in favor of more easily engineered endonucleases. This engineering challenge represents a high barrier to entry and has enabled us to secure a strong intellectual property position and control over what we believe to be a superior genome editing technology.

Other than the key programming challenge, we believed that the differentiated properties of I-CreI cited above made it an ideal "scaffold" for the development of novel genome editing tools. Moreover, we believed those properties were differentiated enough from other editing technologies to merit substantial investment in overcoming the key challenge of programmability. To that end, we invested 15 years of research effort to develop a robust, proprietary protein engineering method that now enables us to consistently re-program I-CreI to direct it to targeted sites in a genome. We call our approach ARCUS.

Our ARCUS Genome Editing Platform

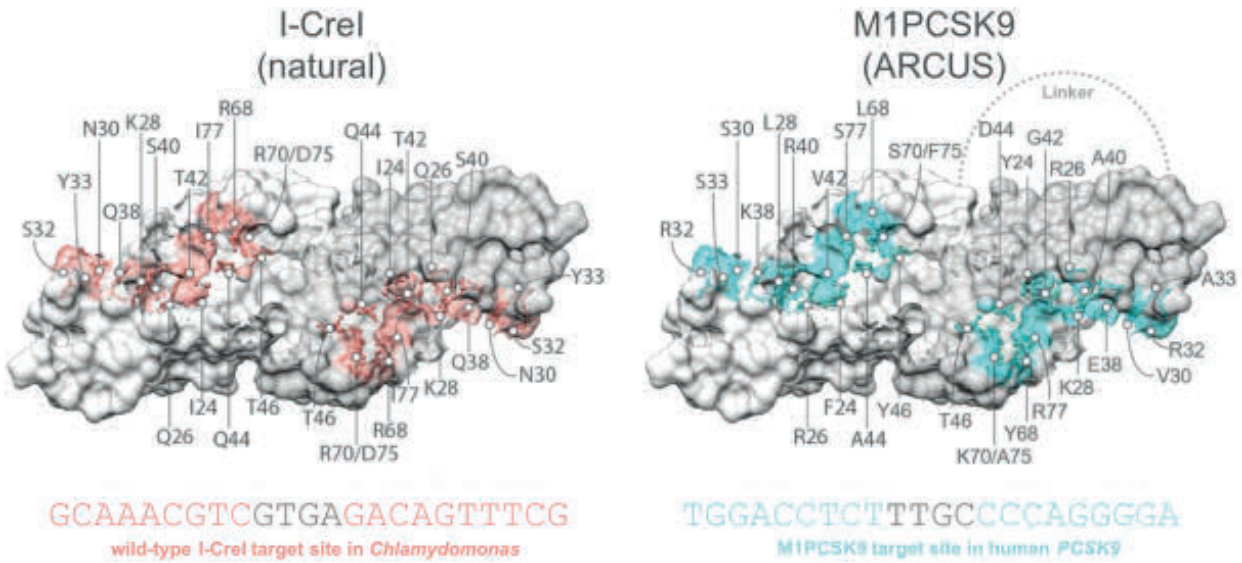
ARCUS is a collection of protein engineering methods that we developed specifically to re-program the DNA recognition properties of I-CreI. In nature, the I-CreI endonuclease recognizes and cuts a DNA sequence in the genome of algae. To apply I-CreI to genome editing in other cells or organisms, we must modify it to recognize and cut a different DNA sequence for each new application we pursue. Since the I-CreI endonuclease evolved to recognize its target sequence in the algae genome with a high degree of selectivity, as supported by scientific literature, it was necessary for us to develop sophisticated protein engineering methods to re-engineer I-CreI endonucleases to bind and cut a different DNA sequence. Using the ARCUS process, we create customized endonucleases for particular applications. We call these custom endonucleases "ARCUS nucleases." Our process is proprietary and core components are claimed in an extensive international patent portfolio. Moreover, since the ARCUS process involves a sophisticated blend of protein engineering art and science, each ARCUS nuclease we create is novel and, we believe, patentable. As of December 31, 2020, we have

obtained U.S. patents with claims directed to six ARCUS nucleases as compositions of matter, and currently claim over 290 ARCUS nucleases as compositions of matter in pending U.S. and foreign patent applications.

Our objective with ARCUS is to redirect I-CreI to a new location in a genome without compromising its editing abilities. To accomplish this, we modify the parts of the enzyme that, as reported by scientific literature, are involved in recognizing the specific DNA target site. These enzyme parts are also reported to comprise the I-CreI active site and to be involved in anchoring the enzyme to its DNA site in the algae genome. In our preclinical studies, we have observed that these modifications allowed us to control how tightly an engineered variant of I-CreI binds to its intended DNA site, as well as how quickly it cuts, in a plant or animal cell. By adjusting these two parameters, we observed that we can generally control the efficiency with which the engineered endonuclease cuts its intended target site or any potential off-target sites.

The natural I-CreI target site is pseudo-palindromic, meaning the first half of the sequence is approximately a mirror image of the second half of the sequence. Palindromic DNA sites are rare in most genomes so it was necessary for us to develop additional technology that would overcome this limitation on the diversity of DNA sites that we can target. To this end, the ARCUS process involves the production of *two* re-programmed I-CreI proteins for each target site. These two different proteins are then linked together into a single protein that can be expressed from a single gene. This approach, called a "single-chain endonuclease," represents a major advancement in I-CreI engineering because it enables our ARCUS nucleases to recognize and cut *non*-palindromic target sites using an endonuclease that, like natural I-CreI, is very small and easy to deliver to cells.

The graphic below depicts the molecular structure of natural I-CreI in comparison to an engineered ARCUS nuclease called "M1PCSK9." The regions of the structures colored in pink or cyan represent the amino acid building blocks that are responsible for contacting the DNA target site and determining the sequence of DNA bases that the endonuclease recognizes and cuts. The DNA target sites recognized by the two endonucleases are shown below the structures.



Since creating an ARCUS nuclease requires such extensive reengineering of I-CreI, it is, generally, an iterative process that involves multiple cycles of design and testing. We can typically produce a first-generation ARCUS nuclease in seven weeks. First-generation nucleases are suitable for research and development, proof-of-concept studies or other non-therapeutic applications. For therapeutic applications requiring the lowest possible off-targeting, however, we are rarely satisfied with generation one and each endonuclease undergoes extensive optimization. To this end, we thoroughly interrogate the nuclease with respect to its on-and off-target cutting properties using ultra-sensitive tests that we developed specifically for use with ARCUS. These results then inform our design of a second-generation nuclease with the goal of optimizing on-target efficiency while minimizing off-target cutting. Therapeutic ARCUS nucleases typically require two to four cycles of design and testing, often resulting in off-target cutting frequencies that are below the limit of detection with our most sensitive assays. This process can take six months or longer and has resulted in development of "therapeutic-grade" editing endonucleases.

The ARCUS process is robust and reproducible. It enables us to create engineered variants of the I-CreI endonuclease that recognize and cut DNA sites that bear little resemblance to I-CreI's natural target site. Importantly, however, ARCUS retains the attributes of I-CreI that we believe make it highly suitable as a genome editing endonuclease for complex commercial applications. We expect ARCUS nucleases to be exquisitely specific as a result of the natural structure of I-CreI and the intricate design process we employ to create them. We believe ARCUS nucleases are the smallest and easiest to deliver genome editing endonucleases. Like I-CreI, in our preclinical studies, ARCUS nucleases have been observed to produce DNA cuts with 3' overhangs that promote HDR, facilitating

gene insertions and gene repairs in addition to gene knockouts. We believe that these attributes will enable us to translate ARCUS into patient-based clinical trials and a wide array of product candidates that have the potential to address the limitations of other genome editing technologies and improve life.

We believe that ARCUS is a leading genome editing platform for therapeutic and food applications. Realizing the potential of ARCUS, however, requires supporting technologies and capabilities. To facilitate the potential commercial deployment of ARCUS in different fields, we surround it with ancillary technologies, domain expertise and infrastructure specific to that area of development. Our goal is to leverage ARCUS to build additional product-development platforms designed to rapidly generate new products in a given field.

Our Allogeneic CAR T Immunotherapy Platform

We are leveraging the properties of ARCUS in an integrated platform for the development and large-scale production of off-the-shelf (allogeneic) CAR T cell immunotherapies. A key to the success of this platform is our proprietary, one-step method for modifying the genetics of T cells from a healthy donor to make them detect and kill cancer cells. This method allows us to produce allogeneic CAR T therapy candidates with a potentially optimal phenotype for clinical development and scaled manufacturing. We have demonstrated that our approach yields an allogeneic product with a high proportion of naïve and central memory CAR T cells, which are the T cell phenotypes that have previously correlated best with good clinical benefit and fewer adverse events compared with terminally differentiated effector T cells. Additionally, because these cells are derived from healthy donors and maintain the phenotypic characteristics described, it is our hypothesis that they will be more capable of controlled *in vivo* expansion and tumor killing without requiring harsh lymphodepletion regimens to be administered to the patient. As such, we believe that our allogeneic CAR T cell platform will greatly increase patient access to these cutting-edge treatments.

CAR T Cell Therapies

CAR T cell therapy is a form of cancer immunotherapy that uses a patient's immune system to kill cancer cells. T cells are a component of the immune system that can distinguish pathogen-infected or tumor cells from healthy cells and kill them. Recognition of pathogen-infected cells or tumor cells occurs through a protein called a TCR, that is expressed on the surface of T cells. Tumor cells, however, have evolved numerous ways to evade TCR-mediated killing by T cells. In CAR T cell therapy, T cells are engineered *ex vivo* to express a protein called a chimeric antigen receptor, or CAR, that recognizes specific tumor cell surface targets and allows the T cells to function independently of the TCR, thus circumventing tumor cells' evasion of the TCR. CAR T cell therapy has been shown in clinical trials to be an effective treatment for patients who have not responded to traditional cancer treatments, and there are now two FDA approved CAR T cell products available to treat certain types of leukemia and lymphoma.

The most common form of CAR T cell therapy, which includes the two approved therapies, is referred to as "autologous" CAR T cell therapy because the CAR T cells are generated using T cells taken directly from the cancer patient. T cells are harvested from the patient, genetically engineered *ex vivo* to express a CAR, and then injected back into the patient. While autologous CAR T cell therapy has been shown to be effective for treating certain tumor types, it has several significant drawbacks:

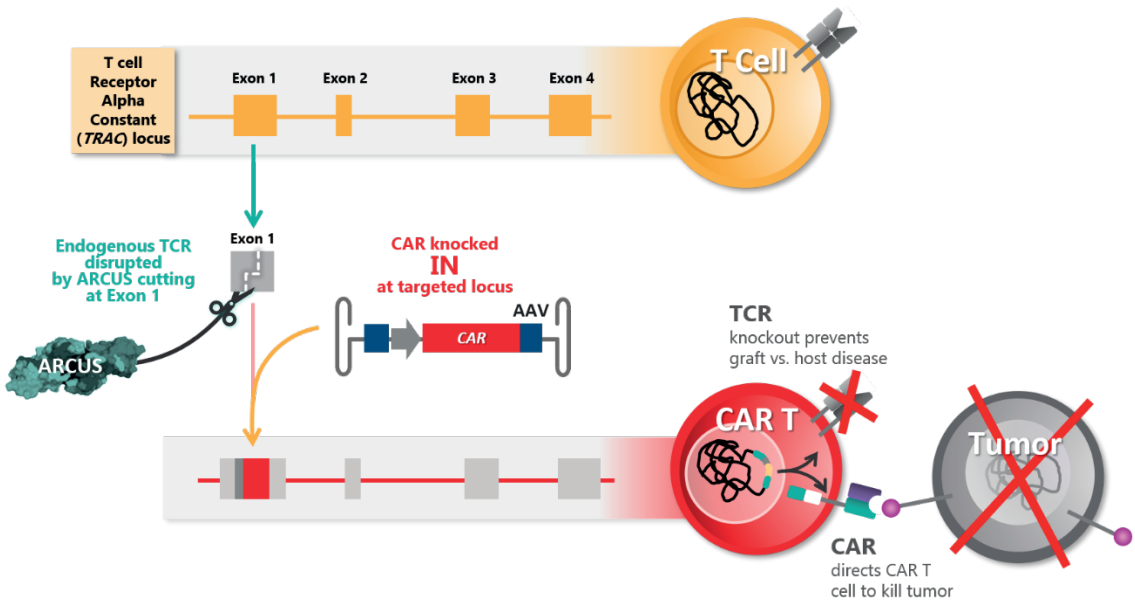
- **Patient eligibility.** Many patients may not be eligible for the treatment because their cancer has lowered their T cell numbers and T cell quality, or because the risk of undergoing the process to harvest T cells is too great.
- **Consistency.** Since each autologous therapy is, by definition, unique, it is difficult to define standards of safety and efficacy or to thoroughly assess the quality of the product prior to infusion into the patient.
- **Delay in treatment.** Because the process to make autologous CAR T cells can take several weeks, there is a significant delay in treating what can often be very aggressive tumors. Patients' disease often progresses before they can receive the CAR T therapy, or if manufacturing complications such as contamination, mislabeling or low yield are encountered, the patient may not survive long enough to attempt manufacturing a second time.
- **Cost.** The autologous CAR T cell manufacturing process is complex and expensive and must be performed, in its entirety, for each patient. As such, scaling of the manufacturing process is exceedingly difficult, and the cost of product manufacturing has resulted in high treatment costs per patient. This high cost of treatment, along with the practical complexities described above, limits the availability of autologous CAR T cell therapies to patients.

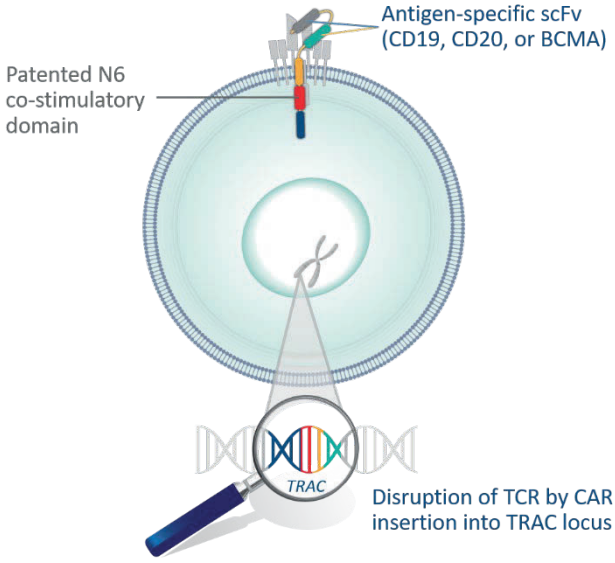
Our Approach to Allogeneic CAR T Cells

We believe that the use of allogeneic, or donor-derived, CAR T cells will address many of the challenges associated with autologous CAR T cell therapy. An allogeneic approach allows selection of donors using specific criteria to define "healthy" T cells possessing specific phenotypes, which we believe are important to clinical efficacy and which may lessen the product-to-product variability seen in autologous therapies. Donor-derived cells could be used in any patient, eliminating the "one patient: one product" burden of autologous CAR T cell therapies. Because healthy donors would provide the starting material, patients that were too sick or otherwise unqualified for an autologous approach may benefit from an allogeneic CAR T cell therapy. Additionally, patients receiving an off-the-shelf allogeneic treatment would not have to wait for the manufacture of a personalized autologous treatment, which could be further delayed by manufacturing difficulties. By scaling the manufacturing of CAR T cells and optimizing the manufacturing process for a specific pool of donors, we believe that allogeneic CAR T cells can be manufactured at costs that are significantly lower than autologous CAR T cells and that will, over time, approach the manufacturing costs for conventional biologic drugs. These potential advantages of an allogeneic approach should allow for a safer, more predictable product with defined quality standards and significantly increase patient access.

We have used the unique qualities of ARCUS to create a one-step cell engineering process for allogeneic CAR T cells that we believe yields a well-defined cell product and is designed to maintain naïve and central memory T cell phenotypes throughout the CAR T manufacturing process; we believe this is of paramount importance for an optimized CAR T therapy. To produce an allogeneic CAR T cell, it is necessary to make two changes to the DNA of T cells from a healthy donor. First, it is necessary to knock out the gene that encodes the TCR to prevent the donor-derived T cells from eliciting GvHD in the patient. The TCR is actually a complex of several different components encoded by different genes, and knocking out any one of them is generally sufficient to prevent the TCR from functioning. Second, it is necessary to add, or knock in, a gene that encodes the CAR to give the T cells the ability to recognize and kill cancer cells. We developed a proprietary, one-step method for achieving both genetic changes simultaneously. This method, aspects of which are protected by nine issued U.S. patents, involves the use of ARCUS to target the insertion of a CAR gene directly into the gene that encodes the alpha subunit of the TCR. This approach adds the DNA encoding the CAR while simultaneously disrupting the DNA encoding the TCR, essentially replacing one gene with the other.

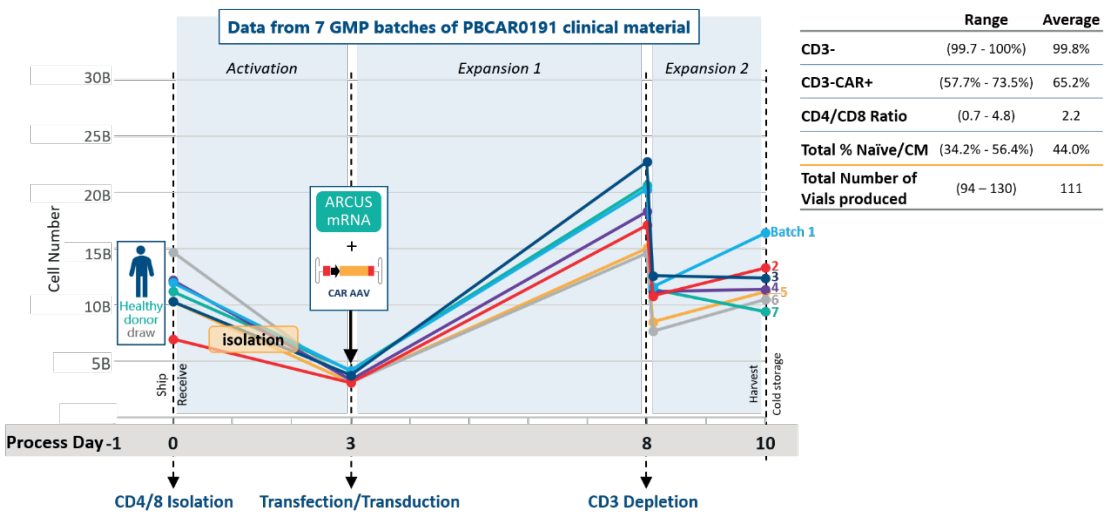
One-step engineered allogeneic CAR T cells





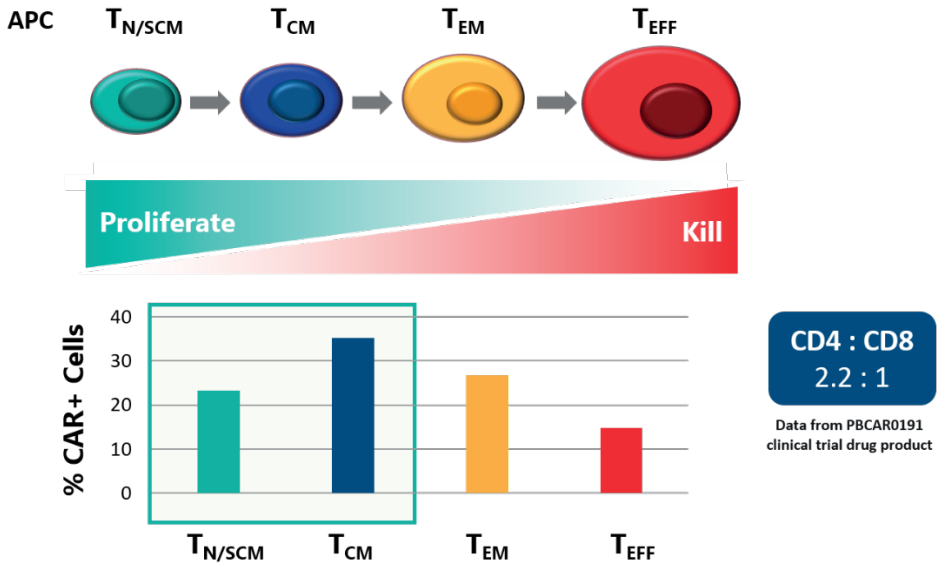
We believe that our one-step engineering approach, and the differentiated attributes of the ARCUS nuclease used to implement it, will overcome many of the critical challenges associated with allogeneic CAR T cell production as follows:

- **T cell phenotype.** According to scientific literature, T cell phenotype has a profound impact on the efficacy of CAR T cell therapy. Specifically, "young" CAR T cells with naïve and central memory phenotypes have been observed to undergo the most robust expansion following administration, which leads to a therapeutic effect. Therefore, we have established a T cell platform that is designed to maximize the percentage of cells with these ideal phenotypes. Our process starts with carefully screening donors to identify individuals with high percentages of naïve or central memory T cells and a ratio of CD4:CD8 T cells that we believe should yield the most potent cell product. To this end, we have developed our own set of analytics for screening candidate donors and have put significant effort into identifying individuals with the desired T cell profiles. We then use proprietary growth strategies and media to maintain naïve and central memory T cell phenotypes throughout the CAR T manufacturing process. We believe this is of paramount importance for an optimized CAR T therapy. Importantly, our one-step genome editing approach avoids making multiple breaks to the T cell's DNA and also contributes to minimizing cell processing time, which helps prevent the CAR T cells from differentiating during the process. We believe our 10-day allogeneic manufacturing process is the shortest established process in the industry. The figure below shows results from seven full-scale manufacturing campaigns, each of which produced a cGMP batch of PBCAR0191 with desired product specifications.

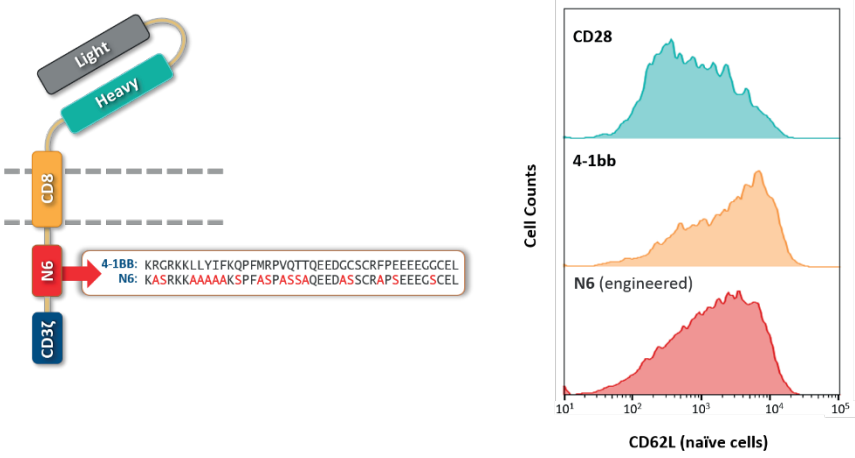


	Range	Average
CD3-	(99.7 - 100%)	99.8%
CD3-CAR+	(57.7% - 73.5%)	65.2%
CD4/CD8 Ratio	(0.7 - 4.8)	2.2
Total % Naïve/CM	(34.2% - 56.4%)	44.0%
Total Number of Vials produced	(94 – 130)	111

The figure below shows phenotype data from PBCAR0191 CAR T cells that were produced as drug product for our ongoing Phase 1/2a clinical trial in adult patients with R/R NHL and R/R B-ALL. The drug product comprises naïve ($T_{N/SCM}$) and central memory (T_{CM}) T cells.



- **Novel co-stimulatory domain.** Our genetically engineered CAR T cells incorporate a novel, proprietary, costimulatory domain called N6, which enables us to enhance cell proliferation and effector function while preserving cell phenotype. We engineered N6 to improve on the function of the 4-1bb costimulatory domain commonly used in autologous CAR T products. Our preclinical data suggests that, compared to 4-1bb, N6 provides an activation signal to the CAR T cells that better preserves cell expansion potential while maintaining naïve cell phenotype following exposure to cancer cells. We also believe N6 can help avoid CAR T cell hyperstimulation, which can contribute to adverse events seen with autologous products.

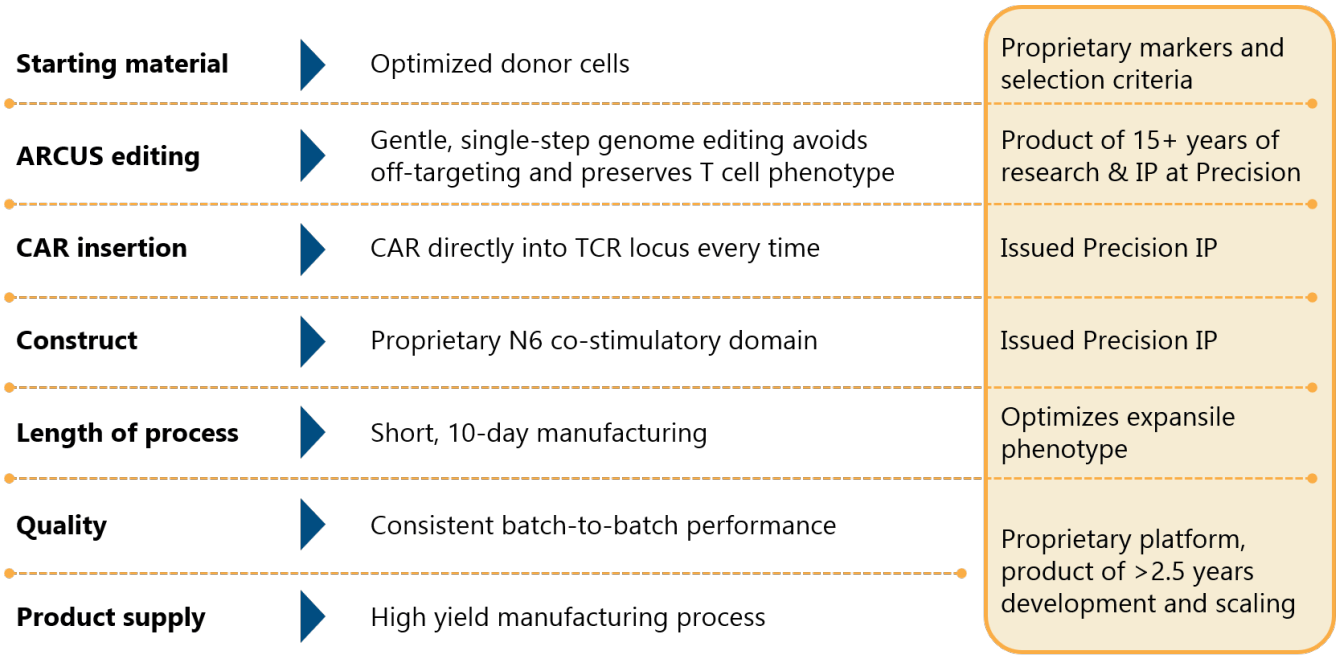


- **Consistency.** By consistently targeting the same insertion of the CAR gene to a defined location in the DNA of the cell, we are able to produce populations of T cells that are identical at the DNA level. This makes the cells in our CAR T cell drug formulation less heterogeneous as compared to manufacturing processes that use lentiviral vectors. Importantly, our genome editing process gives us greater control over the amount of CAR that is expressed on the surface of each CAR T cell, which determines how easily the CAR T cell is activated once it encounters a cancer cell. This allows us to "fine-tune" the CAR T cells to ensure that they respond appropriately to the cancer but do not become hyper-activated or exhausted. The below comparison demonstrates the difference in consistency achieved by using lentivirus delivery compared with targeted delivery through an ARCUS nuclease. CAR T cells produced using ARCUS exhibit reduced cell-to-cell variability as well as more controlled levels of CAR gene expression depending on whether the cells are tuned for high expression or low expression.

- **Scalability.** To realize the potential benefits of allogeneic CAR T cell therapy, it will be important to manufacture as many cells as possible in each batch in accordance with cGMP. Scaling efficiently requires scale-up at every step in the process and, as with all drug manufacturing, process development takes significant time and capital. In July 2019, we opened our

Manufacturing Center for Advanced Therapeutics ("MCAT") facility, which we believe is the first in-house cGMP compliant manufacturing facility dedicated to genome-edited, off-the-shelf CAR T cell therapy product candidates in the United States. We made the decision early in the development of our CAR T cell platform to invest in process development and manufacturing rather than initiating clinical trials with a process that would not fully support development and commercialization. We did this, in part, because we believed that several attributes of ARCUS, such as high specificity and high knock-in efficiency, would allow us to scale manufacturing more effectively than our competitors. As a consequence of our early investment and the one-step editing method enabled by ARCUS, we have scaled our manufacturing process today, adding in-house capabilities through the opening of our MCAT facility. During 2020, we completed technology transfer of PBCAR0191 and PBCAR20A to MCAT, as well as manufactured the first batch and clinical trial material for PBCAR269A and produced clinical trial material for PBCAR19B stealth cell.

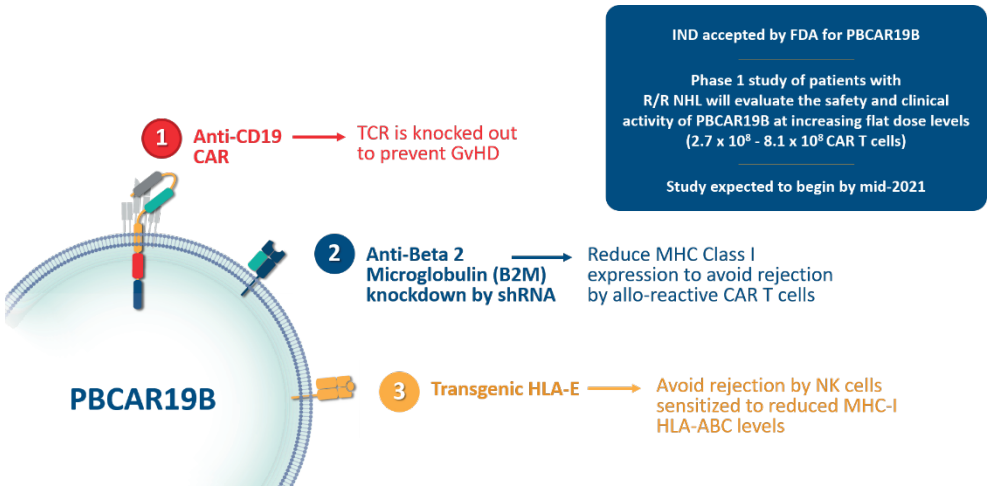
Key features of Precision's allogeneic CAR T platform



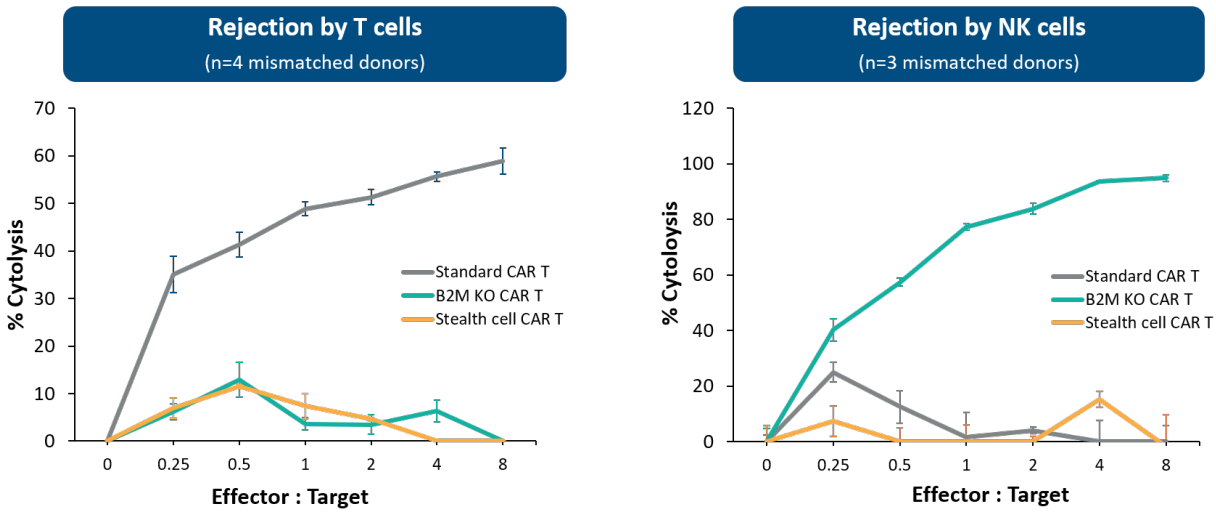
Preventing CAR T Cell Rejection

A patient's immune system is expected to recognize allogeneic CAR T cells as foreign and destroy or reject the cells. This rejection could limit the efficacy of the CAR T therapy if the cells do not persist long enough in the patient to eradicate the tumor. Patients who receive CAR T therapy are typically preconditioned prior to being given the cell therapy using lymphodepleting drugs such as cyclophosphamide or fludarabine, which suppress the immune system of the patient. We believe that the degree of preconditioning can be modified by adjusting the doses of the cyclophosphamide or fludarabine to prevent CAR T cell rejection by patients who receive our treatments due to our unique approach to producing CAR T cells. Our CAR T production process preserves T cell phenotypes that we believe are highly expansile *in vivo* and therefore do not require an aggressive lymphodepletion regime to survive and proliferate in the body.

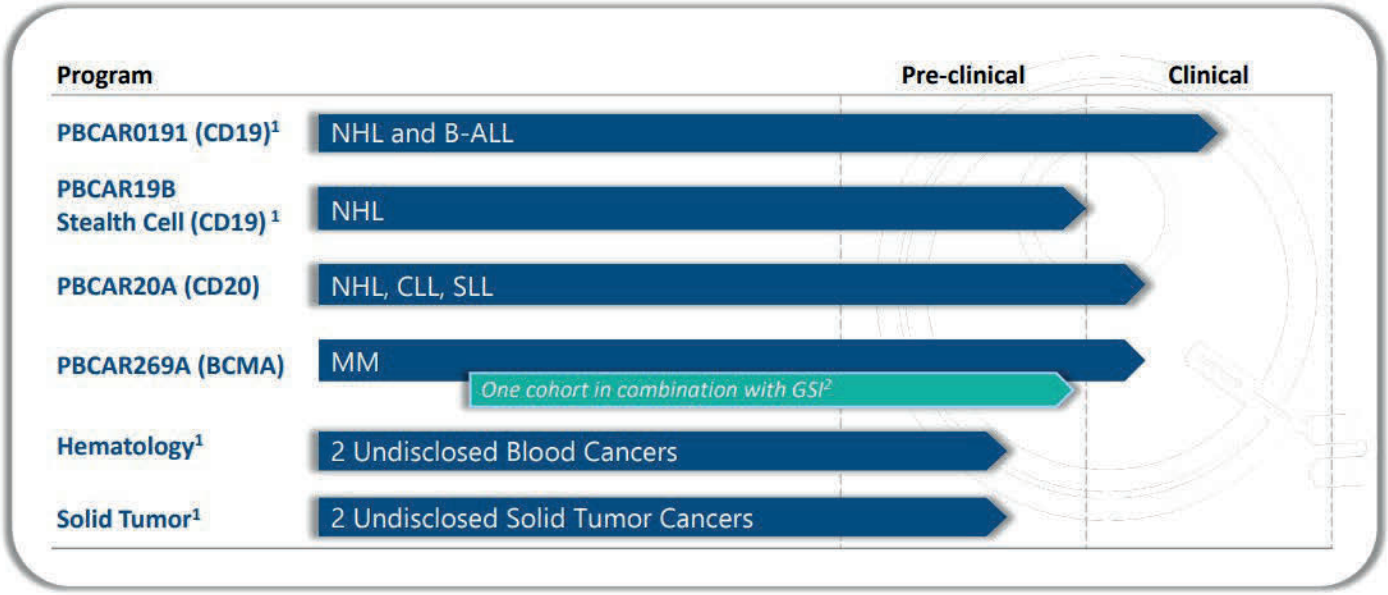
We expect to begin the Phase 1 study of PBCAR19B, our next-generation, stealth cell, CD19 allogenic CAR T candidate for Non-Hodgkin Lymphoma by mid-2021. The stealth cell technology is a modified CAR T vector that is designed to suppress expression of a gene called beta-2-microglobulin, or B2M, in CAR T cells using a short-hairpin RNA, or shRNA, and enable expression of a transgenic HLA-E molecule on the cell surface. B2M is a component of the major histocompatibility complex type 1 ("MHC-I"), a cell surface receptor which enables alloreactive T cell recognition and activation. Suppression of B2M expression leads to reduced cell-surface expression of major histocompatibility complex components HLA-A, HLA-B, and HLA-C. In preclinical studies, we and others have observed that suppression or elimination of B2M reduces the rejection of CAR T cells by alloreactive T cells from an unrelated individual. However, we have found that reduction of cell-surface HLA-A, HLA-B, and HLA-C expression provokes rejection of the CAR T cells by an alternative immune cell called natural killer, or NK cells. Decreased expression of HLA-A, HLA-B, and HLA-C therefore necessitates an additional modification to enable overexpression of HLA-E, a non-classical MHC -I that inhibits cytotoxic killing by NK cells by interacting with inhibitory receptors on the NK cell surface (Gornalusse et al, 2017; Lanza et al, 2019). Thus, the "stealth cell" is designed to avoid rejection by both alloreactive cytotoxic T cells and NK cells, which we believe has the potential to increase the ability of these cells to expand, persist, and mediate anti-tumor activity in unrelated recipients as summarized in the figure below.



Pre-clinical studies showed anti-CD19 stealth CAR T cells resisted rejection by allo-reactive T cells and NKs in mixed-lymphocyte reactions



Our Allogeneic CAR T Immunotherapy Pipeline



[1] In partnership with Servier.
[2] In combination with gamma secretase inhibitor from SpringWorks Therapeutics.

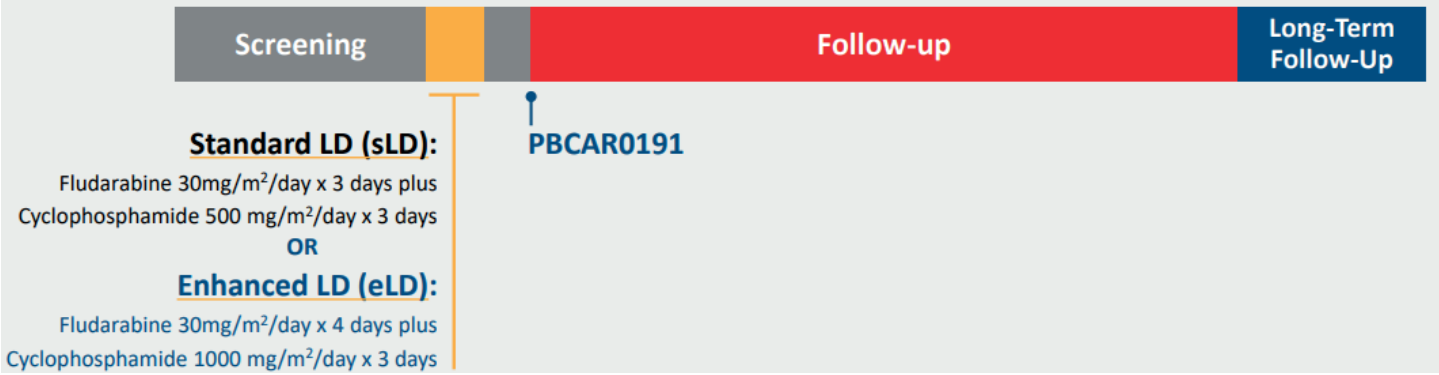
We are leveraging our CAR T cell platform to develop product candidates against validated CAR T cell targets. By focusing on validated targets, we seek to avoid many technical hurdles associated with early clinical development and can validate our allogeneic platform in patients with fewer variables. This approach also allows us to leverage the abundance of available public resources for these targets, including CARs, cell and animal models, and clinical protocols. We believe that our modular CAR T platform will allow us to leverage proof-of-concept from our ongoing and planned initial human trials for multiple other CAR T programs. We believe that we have developed the first allogeneic CAR T cell platform capable of producing drug product at scale, with a potentially optimal cell profile for therapeutic efficacy and true off-the-shelf delivery without the need for harsh and potentially toxic lymphodepletion. We believe that the combination of these factors, along with our next generation ARCUS technology, puts us in a differentiated position to become the leader in the development of allogeneic CAR T therapies.

The first four product candidates in our allogeneic CAR T cell development pipeline are:

- **PBCAR0191**. We are developing PBCAR0191, an allogeneic anti-CD19 CAR T cell product candidate for the treatment of adult R/R NHL and adult R/R B-cell precursor ALL. CD19 is a protein that is expressed on the surface of B cells and is a well-validated target for CAR T cell therapy. The three currently marketed autologous CAR T cell therapy products also target CD19. In February 2016, we entered into the Servier Agreement, pursuant to which we have agreed to develop allogeneic CAR T cell therapies for CD19.

We are currently evaluating patients in a Phase 1/2a clinical trial of PBCAR0191 in adult patients with R/R NHL or R/R B-cell precursor ALL, the trial design of which is shown in the figure below. The primary objective of this trial is to evaluate the safety and tolerability of PBCAR0191, as well as to determine the maximum tolerated dose. Secondary objectives include evaluating the anti-tumor activity of PBCAR0191. We are also evaluating the expansion, trafficking and persistence of PBCAR0191 in this trial. NHL and ALL cohorts are evaluated independently. The base trial design included up to three dose levels: 3.0×10^5 cells/kg, 1.0×10^6 cells/kg and 3.0×10^6 cells/kg. Recently, we have added higher dose levels in flat doses (DL4b: 500×10^6 cells and DL5: 750×10^6 cells). Patients will be further evaluated for a follow-up period of 11 months. Additionally, alternative lymphodepletion regimens, including enhanced doses of fludarabine and cyclophosphamide, are also being explored. Finally, repeat dosing after initial response

and progression and scheduled repeat dosing, both with repeat lymphodepletion, are also being explored. The trial is being conducted at the multiple sites around the United States. A listing of these sites can be found at https://clinicaltrials.gov/ct2/show/NCT03666000.



Updated Interim Data from Phase 1/2a Trial of PBCAR0191 in R/R NHL and R/R B-ALL

In December 2020, we reported updated interim data from our ongoing Phase 1/2a clinical trial of PBCAR0191. As of the November 16, 2020 cutoff, 27 patients including 16 patients with R/R NHL and 11 patients with R/R B-ALL had been enrolled and evaluated. For this study, in which patients received either sLD or eLD, response rates across R/R NHL and R/R B-ALL patient cohorts were as follows:

- 83% objective response rate ("ORR") at day 28 or later for patients across NHL (n=4) and B-ALL (n=2) who received PBCAR0191 when coupled with eLD.
- At day 28 or later, 75% (3/4) of NHL patients who received PBCAR0191 with eLD achieved a complete response ("CR"). Meanwhile, 33% of NHL patients (n=9) across DL2 and DL3 using sLD achieved a CR.
- The longest demonstrated response was > 11 months in a B-ALL patient at DL2.

Response Rates at Day ≥28	NHL (n=16)		B-ALL (n=11)	
	ORR	**CR**	**ORR**	**CR**
DL1 ($3x10^5$ cells) + sLD	67% (2/3)	0% (0/3)	-	-
DL2 ($1x10^6$ cells) + sLD	67% (2/3)	33% (1/3)	33% (1/3)	33% (1/3)
DL3 ($3x10^6$ cells) + sLD	50% (3/6)	33% (2/6)	25% (1/4)	25% (1/4)
DL4 (2 doses at $3x10^6$ cells) + sLD	-	-	50% (1/2)	50% (1/2)
Enhanced LD Regimen	100% (4/4)	75% (3/4)	50% (1/2)	50% (1/2)

PBCAR0191, which incorporates our patented N6 co-stimulatory domain, demonstrated a clear dose dependent increase in peak cell expansion. Compared to sLD, patients undergoing eLD with PBCAR0191 at DL3 resulted in approximately 95-fold increase in peak cell expansion, and approximately 45-fold increase in area under the curve. This was associated with a higher CR rate in NHL (75%). In this dose escalation and dose expansion study, PBCAR0191 had an acceptable safety profile with no cases of graft versus host disease, no cases of Grade ≥ 3 cytokine release syndrome, and no cases of Grade ≥ 3 immune effector cell neurotoxicity.

One NHL patient who was treated with PBCAR0191 and eLD had previously received nine prior lines of therapy before entering the trial. The patient presented with persistent cytopenias at baseline and a history of infections, including bacterial sepsis. The patient had an episode of sepsis at day 27 which appeared to have resolved at day 33, following which a partial response was achieved at day 34. Unfortunately, the patient died at day 42 with grade 5 sepsis. We reported the serious adverse event to the FDA and reported the patient death.

We are enrolling additional patients with eLD and plan to present updated interim data on this study by mid-2021.

Additionally, the FDA has accepted our IND application for PBCAR19B, our next-generation, stealth cell, CD19 allogeneic CAR T candidate for Non-Hodgkin Lymphoma, and we expect to begin the Phase 1 study by mid-2021. In preclinical studies, PBCAR19B has been shown to delay both T cell and natural killer cell mediated allogeneic rejection *in vitro* and may improve the persistence of allogeneic CAR T cells in recipients after infusion.

PBCAR20A. Our second allogeneic CAR T therapy candidate is PBCAR20A, an allogeneic anti-CD20 CAR T cell product candidate for the treatment of NHL, including chronic lymphocytic leukemia, or CLL, and small lymphocytic lymphoma, or SLL. Like CD19, CD20 is a protein expressed on the surface of B cells. It is a validated target for cancer treatment and several CD20-targeted therapies, such as the monoclonal antibody Rituxan, have long histories of clinical and commercial success. In April 2020, we commenced patient dosing in a Phase 1/2a clinical trial of PBCAR20A. The trial will include patients with NHL, of which a subset will have the diagnosis of mantle cell lymphoma, or MCL. We have received orphan drug designation for the treatment of MCL.

In our Phase 1/2a clinical trial, the primary objective is to evaluate the safety and tolerability of PBCAR20A, as well as to determine the maximum tolerated dose. Secondary objectives will include evaluating the anti-tumor activity of PBCAR20A. We also plan to evaluate the expansion, trafficking and persistence of PBCAR20A in this trial. Based on the safety profile observed to date with PBCAR0191, the FDA allowed us to commence dosing with PBCAR20A directly at 1 x 10^6 cells/kg. The study has continued to dose escalate through dose level two (3 x 10^6 cells/kg), and in February 2021, we commenced patient dosing at dose level 3 (480 x 10^6 cell fixed dose) with a max dose of 6 x 10^6 cells/kg. We expect to report interim data for the PBCAR20A study in 2021.

Our accepted IND for PBCAR20A included data from our preclinical study in mice measuring cell proliferation, cytotoxic killing, and production of effector cytokines in response to co-culture with CD20+ or CD20- target cells. PBCAR20A CAR T cells were observed to proliferate in response to stimulation by CD20+ K20 cells (K562 myelogenous leukemia cells transfected to express human CD20) at a wide range of doses (effector to target ratios ranging from 1:1 to 1:9). These observations show that, in this study, PBCAR20A cells became activated by and killed CD20+ cells at a wide range of cell doses. In this study, we observed that PBCAR20A cells did not proliferate in response to co-culture with CD20 negative cell K562 cells.

We also evaluated the potency of PBCAR20A *in vivo*. PBCAR20A was observed to prolong survival in a mouse model of lymphoma (Raji Sub-Q model) at both doses tested (1.0 x 10^6 and 5.0 x 10^6 cells per mouse), which we believe supports further development. PBCAR20A was observed to be well-tolerated in this study.

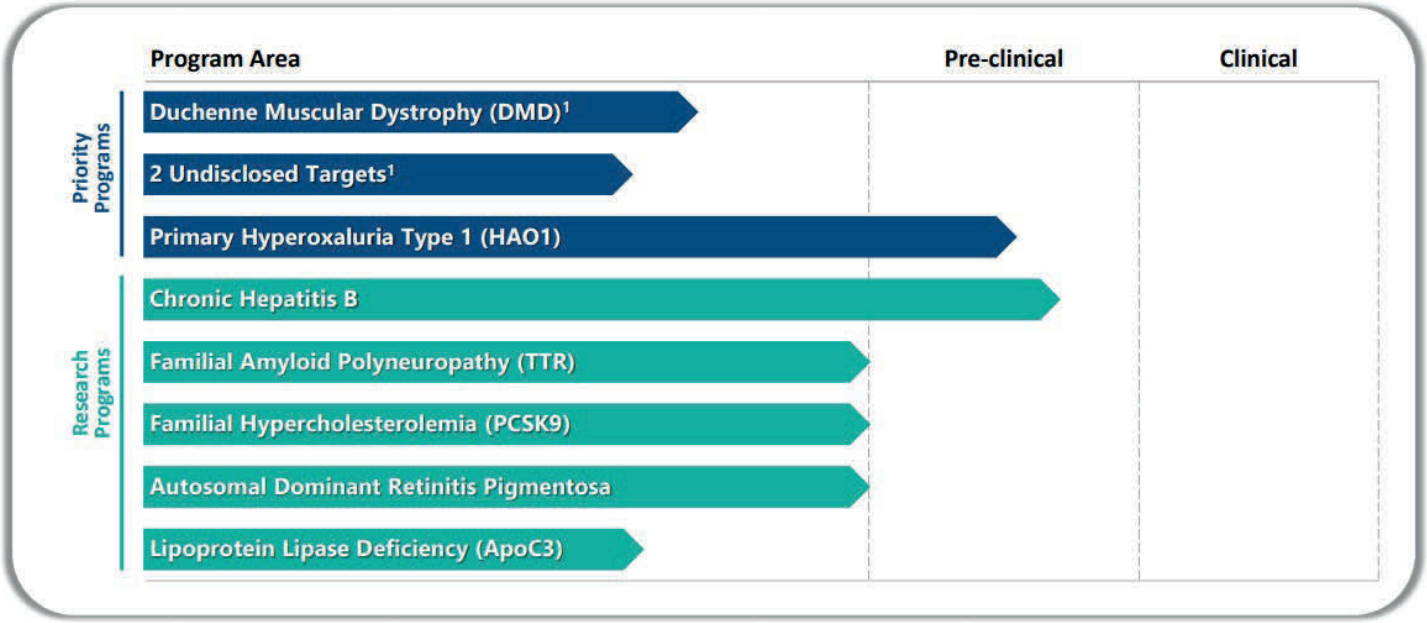
PBCAR269A. We are developing PBCAR269A as an allogeneic anti-BCMA CAR T cell product candidate for the treatment of R/R multiple myeloma. BCMA is a protein that is expressed on the surface of mature B cells called “plasma cells” that are responsible for the disease and is a validated CAR T cell target. In January 2020, the FDA cleared our IND for PBCAR269A.

In June 2020, we commenced a Phase 1/2a open-label, multi-center, dose-escalation clinical trial in patients with R/R multiple myeloma. In this trial, the primary objective will be to evaluate the safety and tolerability of PBCAR269A, as well as to determine the maximum tolerated dose. Secondary objectives will include evaluating the anti-tumor activity of PBCAR269A. We also plan to evaluate the expansion, trafficking and persistence of PBCAR269A in this trial. We expect to investigate up to three dose levels: 6.0 x 10^5 cells/kg, 2.0 x 10^6 cells/kg and 6.0 x 10^6 cells/kg and we expect to report interim data on the PBCAR269A trial in 2021.

We evaluated the potency of PBCAR269A CAR T cells in a preclinical study in mice by measuring cell proliferation, cytotoxic killing and production of effector cytokines in response to co-culture with BCMA+ or BCMA- target cells. In this study, PBCAR269A CAR T cells were observed to proliferate in response to stimulation by BCMA+ target cells including MM.1S (a human multiple myeloma cell line) and KBCMA (K562 myelogenous leukemia cells transfected to express human BCMA) at a wide range of doses (effector to target ratios ranging from 1:1 to 1:8). These observations show that, in this study, PBCAR269A cells became activated by and killed BCMA+ cells at a wide range of cell doses. We further observed that PBCAR269A cells did not proliferate in response to co-culture with BCMA- K562 cells.

We also evaluated the potency of PBCAR269A *in vivo*. PBCAR269A was observed to prolong survival in a mouse model of multiple myeloma, which we believe supports further development. PBCAR269A was observed to be well-tolerated in this study.

Our *in vivo* Gene Correction Platform



[1] In partnership with Lilly

Overview

We expect *in vivo* genome editing to be a significant focus of our operations long-term because the differentiated attributes of ARCUS are particularly advantageous for this type of application. *In vivo* gene correction involves the delivery of ARCUS nucleases directly into a patient's cells to treat disease at the level of the underlying DNA. *In vivo* genome editing is more complex and challenging than *ex vivo* approaches like CAR T cells due to the need to safely deliver ARCUS directly to cells in the body. We believe that *in vivo* applications are particularly well suited to ARCUS because they require extremely low levels of off-target editing and efficient delivery.

Due to the demands of *in vivo* editing, we are taking a highly disciplined approach to managing our project portfolio that emphasizes studies in large animals, using both viral and non-viral delivery technologies. Thus, we are generating a large animal dataset that, we believe, is the most comprehensive of any in the field. Our two most advanced programs in this area are focused on PH1 which we wholly own and DMD in partnership with Lilly.

Treatment of Genetic Disease

Genetic diseases are caused by errors in the DNA that lead to dysfunction of a cell or tissue. While the underlying cause of a particular genetic disease can often be complex and variable, DNA errors generally fall into two categories: loss-of-function or gain-of-function. Genetic diseases are most frequently caused by loss-of-function errors in which a particular gene is mutated at the DNA level in such a way that it is either non-functional or less functional than it should be. In these cases, treating the disease requires *adding* the function that the cell or tissue is otherwise lacking. Gain of function genetic disorders are the result of DNA errors that cause a gene to acquire a new, harmful function that leads to disease. In these cases, it is necessary to remove the unwanted function to treat the disorder.

Genetic disease is a very active area of therapeutic development, and the therapies that are available or in development are, to a large extent, as variable and specialized as the diseases themselves. There are, however, gene therapy platform approaches that are being broadly applied to the treatment of multiple genetic disorders. For the treatment of loss-of-function diseases, AAV-based gene therapy can often be an effective treatment. AAV is a non-integrating virus that can be used to deliver DNA to a wide range of different cell types in a patient. The virus can be engineered to deliver a functional copy of a gene that is otherwise missing or under-performing in the cell. This approach can, in some cases, restore normal function to the cell and alleviate the symptoms of the disease.

While a number of AAV-based gene therapies appear to be showing great promise in clinical trials, the approach is subject to a number of limitations. Many patients have antibodies in their blood that recognize and inactivate the AAV virus before it can deliver the DNA into the patient's cells. In addition, among patients who do *not* have antibodies upon initial treatment with the virus, most will develop antibodies following the first dose. Therefore, in most cases, it is only possible to dose a patient one time. Most importantly, although AAV-based gene therapy can be an effective treatment, it is probably not a permanent *cure* because AAV-delivered genes do not generally persist for more than a few years in the body. While the duration of virus persistence varies from cell-to-cell and from patient-to-patient, it is not believed to be permanent and symptoms of the disease can return once the virus is no longer present in the body.

Our Approach to in vivo Gene Correction

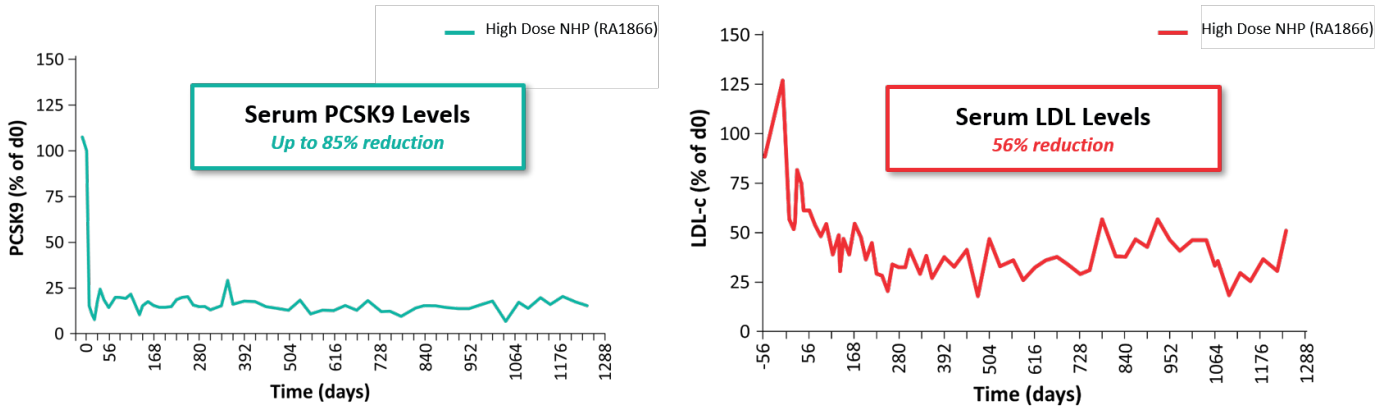
Our goal is to cure genetic diseases by correcting the DNA errors responsible for causing them. In principle, *in vivo* genome editing can likely be used to cure any genetic disorder. In practice, however, *in vivo* genome editing is limited by several challenges that, we believe, are best addressed using ARCUS:

- **Specificity.** *In vivo* genome editing requires an extremely high degree of precision to minimize the occurrence of any unwanted off-target editing. Off-target changes to the DNA could, potentially, have significant safety implications that may not manifest themselves until well after administration of the therapy. As described above, we believe that the differentiated attributes of ARCUS enable us to create endonucleases that have a high degree of specificity and minimal levels of off-target editing to address this significant safety concern.
- **Delivery.** Gene therapy delivery technologies suitable for the delivery of genome editing tools to tissues *in vivo* have not been developed for all tissues. Delivery challenges are particularly pronounced for editing applications that require promoting DNA repair by HDR because it is necessary to deliver both the nuclease and the DNA "donor" template for HDR. We have focused our initial development efforts on genetic disorders of the liver and eye, two tissues for which we believe we have good options for delivery and in which we have shown ARCUS to be effective in preclinical studies. We believe the small size of our ARCUS nucleases and their ability to efficiently promote HDR will enable us to address a greater variety of genetic diseases requiring more complex delivery strategies.
- **Efficiency.** Genome editing efficiency is a critical parameter for *in vivo* therapeutic efficacy because the requisite edit must be achieved in a sufficient number of cells to have therapeutic benefit. Efficiency is best measured *in vivo* in animals because it is affected by multiple parameters including delivery, endonuclease activity and the accessibility of the DNA target site in the organism. Moreover, we believe that only large animals such as NHPs accurately model these different parameters and are representative of the human condition. As such, we have placed significant emphasis on large animal studies and have demonstrated, we believe, therapeutic levels of editing efficiency using ARCUS in the most relevant models. This gives us greater confidence that ARCUS will translate from the lab bench to the clinic.

The potential of ARCUS for *in vivo* genome editing is highlighted in a July 2018 publication in *Nature Biotechnology* that describes a research project performed as part of a sponsored research collaboration between our company with Dr. Jim Wilson and the Gene Therapy Program at the University of Pennsylvania. Co-authors of the publication include Derek Jantz and Jeff Smith, two of our co-founders. This publication is, to our knowledge, the first peer-reviewed publication of *in vivo* genome editing data in NHPs. We reported well-tolerated, long-term, high-efficiency editing of the PCSK9 gene in NHPs using ARCUS. A single IV administration of an AAV vector encoding a PCSK9-specific ARCUS nuclease was able to efficiently knock out the gene in the livers of Rhesus macaques, a species of monkey. Importantly, even at the highest dose the treatment was observed to be well tolerated in the study.

As published in *Molecular Therapy* in February 2021, we have continued to monitor the NHPs for more than three years and have continued to show a sustained reduction in LDL cholesterol levels while maintaining stable gene editing without any obvious adverse effects. After the one-time vector administration more than three years ago, NHPs treated with ARCUS have experienced stable reductions of up to 85% in PCSK9 protein levels and a 56% reduction of LDL cholesterol levels.

PCSK9 and LDL Serum Levels



[1]Wang et al, *Molecular Therapy*, 2021.

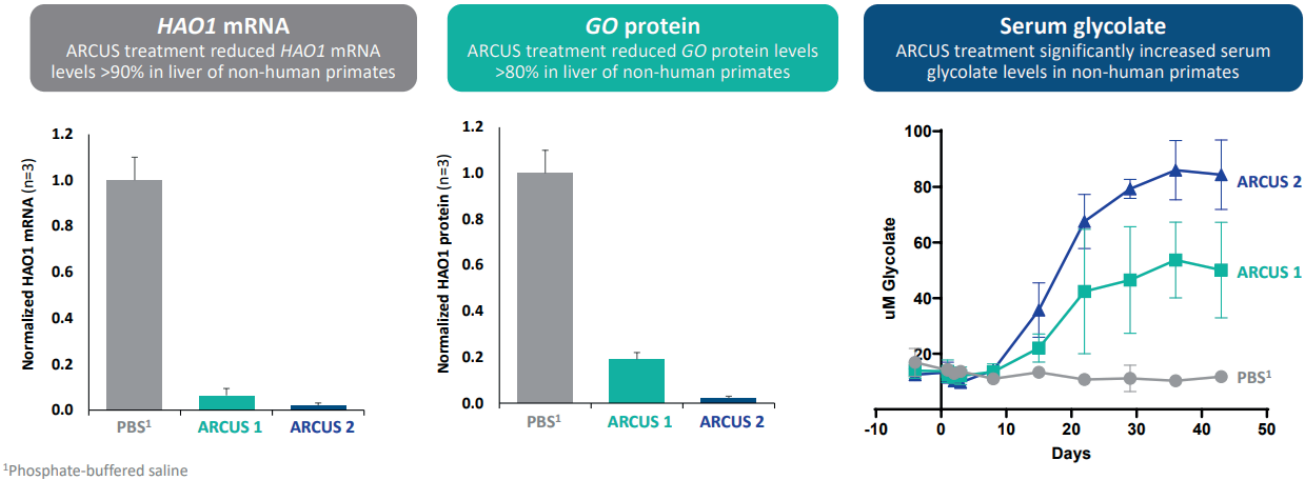
We believe that establishing collaborations with other groups that have additive domain expertise and access to the most relevant animal models will be important to advancing our *in vivo* gene correction platform, and we have entered into a number of collaborations and licensing agreements with third parties to help us advance our *in vivo* editing portfolio.

Primary Hyperoxaluria Type 1 (PH1) Program

We plan to advance a program designed to target the rare genetic disease PH1 as our lead wholly owned *in vivo* gene correction program. PH1 affects approximately 1-3 people per million in the United States and is caused by loss of function mutations in the AGXT gene. This gene encodes an enzyme which is involved in the production of the amino acid glycine in the liver. In patients with PH1 who lack this enzyme, crystals of calcium oxalate form in the kidneys leading to painful kidney stones which may ultimately lead to renal failure. Approximately 40% of PH1 patients are found to have already progressed to end stage renal disease at the point of diagnosis, requiring a combined liver-kidney transplant.

Using ARCUS, we are developing a potential therapeutic approach to PH1 that involves knocking out a gene called HAO1 which acts upstream of AGXT. Suppressing HAO1 has been shown in preclinical models to prevent the formation of calcium oxalate. We therefore believe that a one-time administration of an ARCUS nuclease targeting HAO1 may be a viable strategy for a durable treatment of PH1 patients.

In preclinical studies we have demonstrated that ARCUS efficiently knocked out the HAO1 gene in NHPs. We have also demonstrated in a mouse model of PH1 that administration of an ARCUS nuclease targeting HAO1 resulted in approximately 70% reduction in urine calcium oxalate levels. We have also demonstrated that ARCUS efficiently reduced HAO1 mRNA levels by greater than 90% in the liver of NHPs. Pre-clinical research has continued to progress, and we expect to provide an update on this program in the first half of 2021.



Manufacturing

We believe that we have strong internal scientific process development and manufacturing capabilities, including our MCAT, an in-house cGMP compliant manufacturing facility supporting our therapeutic product development platforms which we opened in 2019. We believe that MCAT is the first in-house cGMP compliant manufacturing facility in the United States dedicated to genome-edited, off-the-shelf CAR T cell therapy products. We believe that having internal manufacturing capacity and expertise is a competitive advantage that enables enhanced control over process development timelines, costs and intellectual property.

We have leased over 33,800 square feet of space for our MCAT facility at a location approximately seven miles from our headquarters in Durham, North Carolina. We have four cleanroom production suites for CAR T cell, mRNA and AAV production for process development for our allogeneic CAR T immunotherapy platform. Our manufacturing facility leverages single-use, disposable, closed-system operations aligned to our technology platforms to ensure both flexibility and cost effectiveness. The initial scope is creating clinical trial material for certain of our planned clinical trials. In the longer term, we believe MCAT has the potential to be a commercial launch facility. During 2020, we completed tech transfer of PBCAR0191 and PBCAR20A to MCAT, as well as manufactured the first batch and clinical trial material for PBCAR269A and produced clinical trial material for PBCAR19B stealth cell.

We currently contract with third parties for the manufacturing of materials used in the production of our product candidates. To date, our third-party manufacturers have met our manufacturing requirements. We believe that there are alternate sources of supply that can satisfy our requirements.

The manufacturing process for our allogeneic CAR T immunotherapy platform utilizes a one-step cell engineering method in which a CAR gene is targeted directly into the TRAC locus. We believe this approach greatly streamlines the manufacturing process and have entered into a license agreement with a principal supplier for research and clinical licensed technology used in such process. Commercial raw materials and reagents for this production are readily available. Our manufacturing strategy for our *in vivo* gene correction platform and our food platform is to internally control process development and manufacturing to safeguard the proprietary nature of our technology and facilitate our ability to function as an integrated life sciences company.

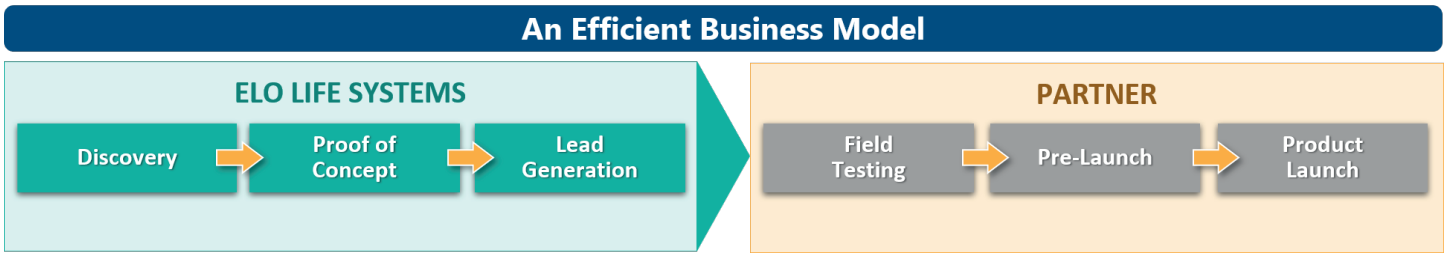
Our Food Platform

Technology-Centric Solutions to Meet Changing Demands in Food and Agriculture

The total global food and agriculture market, estimated to be worth $5 trillion (2015), is heavily influenced by the availability of critical raw material ingredients and changing consumer behavior. With the global population projected to reach 8.5 billion by 2030, demand for basic food and nutrition needs has already put a lot of pressure on traditional food production systems. Many staple foods and critical ingredients, such as citrus, bananas and coffee, are under threat from environmental changes and the new pathogens it can bring. The food and agriculture industry has also seen significant shifts in consumer preferences in which consumers are actively transitioning to high quality and healthier foods and beverages, while rejecting artificial ingredients, sugar and salt, creating a demand for natural and holistic ingredients built on a sustainable supply chain. Traditional approaches to agricultural innovation are slow, siloed, rely heavily on non-scalable academic advancements and continue to use inefficient crop improvement practices. We believe that many of the current pressures on the food and agriculture industry from climate-related threats and changing consumer preferences can be effectively addressed using biotechnology.

Elo Life Systems: Innovation-Focused Technology Platform and Business Model

Elo Life Systems is our wholly owned subsidiary, dedicated to addressing the needs of consumers and consumer-facing industries in the food and agriculture sector. Our business model is heavily partner-focused. In the food and agriculture industry, timelines to market are long and the field is dominated by a relatively small number of entrenched companies. Therefore, it is a very difficult to bring a product to market without a larger partner. Thus, we seek partnerships early in the product development process to optimize our chances of market success. Under this partnership model, we are responsible for the early phases of the project, starting from concept through production of a "lead," which is typically a gene edited plant that has the desired trait in greenhouse testing and is ready for scale-up and testing in the field. At that point, our partners typically assume responsibility for subsequent development and commercialization. In general, our partners are responsible for financing all or a portion of our development costs, which greatly reduces our capital requirements. We are then generally eligible to share in revenues derived from successfully commercialized products developed under these partnerships.



Elo's Technology Platform

At the core of our food platform is our ARCUS editing technology. We are one of the first to apply genome editing technology to crop plants and we believe we have the most in-depth experience in crop genome editing in the industry. Over the last decade, we have developed highly efficient methods to improve delivery and functionality of ARCUS nucleases in plants to edit DNA. These nucleases have been successfully validated in collaborative projects with major food and agriculture companies like Dole, Cargill, BASF, Bayer CropScience and DuPont Pioneer Hi-bred. Importantly, ARCUS can be used to create small deletions or insertions in plants using a non-plant pest- or pathogen-based delivery approach. As such, we believe that many of the food and agriculture product candidates we may develop have the potential to obtain nonregulated status in the United States and other territories and thereby avoid GMO labels. This aspect of the technology platform is critical to food producers, particularly as they respond to consumer demands for healthier products. In addition to ARCUS, Elo's in-house capabilities include:

- **Genomics.** Many of the most attractive opportunities for Elo involve emerging and under-studied crops, such as stevia and monk fruit. We have integrated genome sequencing and bioinformatic platforms in-house in order to identify the genome sequence of plants, enabling us to identify targets for editing with ARCUS nucleases.
- **Target discovery and validation.** Our informatics platform is built on principles of machine learning that allow us to synthesize, sequence and phenotype information from both public and internal datasets to correlate genome sequence with plant characteristics. This allows us to identify genetic targets for ARCUS editing that are predicted to yield a desired phenotype. These targets can then be validated in specific crops and at least partially validated in model systems such as tobacco and Arabidopsis using different molecular approaches such as editing or RNAi.
- **Multi-crop transformation.** Most of the crops of interest to Elo and our partners do not have established transformation protocols and are not readily amenable to gene editing. To this end, we have developed a sophisticated collection of plant transformation vectors and protocols over the last decade that allow us to rapidly develop gene-edited variants of otherwise intractable species. This technology allows us to overcome what is otherwise a significant barrier to entry into a new crop species.
- **Plant growth infrastructure.** Elo has a dedicated facility and capabilities of cultivating gene edited plants from incubator to greenhouse.

Fusarium wilt resistant banana varieties (in collaboration with Dole Food Company)

Fusarium wilt, caused by the Tropical Race 4 (TR4) strain of a plant pathogenic fungus called Fusarium, is a fast-spreading pandemic threatening the continued cultivation of the world's most popular fruit in a $25 billion banana industry. The disease was detected in Colombia in August 2019 and is expected to spread throughout Latin America.

Through our collaboration agreement with Dole, Elo intends to use its proprietary suite of tools, including cutting-edge knowledge mining platform, gene discovery pipeline, trait validation workflows, and end-to-end expertise in translational agriculture, in

combination with its proprietary homing endonuclease-based genome editing platform to develop potential TR4-resistant banana varieties in this important clonally propagated crop.

Plant-Based Proteins

In 2018, we launched Elo Life Systems Australia, a subsidiary of Elo that will support research programs in Australia. Elo Life Systems Australia's primary focus is developing climate-resilient legumes with improved protein and nutritional profiles, starting with chickpea. Multiple edited events in chickpeas have been generated and are being screened in the laboratory. Through this program, we aim for the resulting products to make a significant contribution towards the increasing demand for sustainable plant-based proteins as a healthful alternative to animal protein.

License and Collaboration Agreements

Eli Lilly and Company

In November 2020, we entered into a research collaboration and exclusive license agreement (the "Development and License Agreement") with Lilly to utilize ARCUS for the research and development of potential *in vivo* therapies for genetic disorders. Lilly has initially nominated DMD and two gene targets for other genetic disorders, and has the right to nominate up to three additional gene targets for genetic disorders over the first four years of the Development and License Agreement (the "Nomination Period"). Lilly may extend the Nomination Period for an additional two years from the date on which such initial Nomination Period ends, upon Lilly's election and payment of an extension fee. Under the terms of the Development and License Agreement, Lilly will receive an exclusive license to research, develop, manufacture and commercialize the resulting licensed products to diagnose, prevent and treat any and all diseases by in vivo gene editing directed against the applicable gene target. The Development and License Agreement provides that we will be responsible for conducting certain pre-clinical research and IND-enabling activities with respect to the gene targets nominated by Lilly to be subject to the collaboration, including manufacture of initial clinical trial material for the first licensed product. Lilly will be responsible for, and must use commercially reasonable efforts with respect to, conducting clinical development and commercialization activities for licensed products resulting from the collaboration, and may engage us for additional clinical and/or initial commercial manufacture of licensed products.

In January 2021, we and Lilly closed the Development and License Agreement following clearance under the Hart-Scott Rodino Antitrust Improvements Act of 1976, as amended (the "HSR Act"). In connection with the closing, we received an upfront cash payment of $100.0 million as well as $35.0 million from Lilly's purchase of 3,762,190 newly issued shares of our common stock pursuant to a stock purchase agreement as described below (the "Stock Purchase Agreement"). These cash receipts are not included in the cash and cash equivalents portion of the audited consolidated balance sheet included elsewhere in this Annual Report on Form 10-K. We will also be eligible to receive milestone payments of up to an aggregate of $420 million per licensed product as well as nomination fees for additional targets and certain research funding. If licensed products resulting from the collaboration are approved and sold, we will also be entitled to receive tiered royalties ranging from the mid-single digit percentages to the low-teens percentages on world-wide net sales of the licensed products, subject to customary potential reductions. Lilly's obligation to pay royalties to us expires on a country-by-country and licensed product-by-licensed product basis, upon the latest to occur of certain events related to expiration of patents, regulatory exclusivity or a period of ten years following first commercial sale of the licensed product.

We have the right to elect to co-fund the clinical development of one licensed product, which may be selected from among the third or any subsequent licensed products to reach IND filing. If we elect to co-fund such licensed product, we would reimburse Lilly for a portion of the clinical development expenses for such product and, in exchange, each royalty tier with respect to net sales of such licensed product would be increased by a low single digit percentage. During the term of the Development and License Agreement, we may not (and may not license or collaborate with any third party to) research, develop, or commercialize any *in vivo* gene editing product directed against any gene targets that have been nominated and are subject to the Development and License Agreement.

Unless earlier terminated, the Development and License Agreement will remain in effect on a licensed product-by-licensed product and country-by-country basis until the expiration of a defined royalty term for each licensed product and country. Lilly has the right to terminate the Development and License Agreement for convenience by providing advance notice to us. Either party may terminate the Development and License Agreement (i) for material breach by the other party and a failure to cure such breach within the time period specified in the agreement or (ii) due to a challenge to its patents brought by the other party.

Servier

In February 2016, as further described above, we entered into the Servier Agreement. Pursuant to this Servier Agreement, we have agreed to develop allogeneic chimeric antigen receptor T cell therapies for five unique antigen targets. Servier selected one target at the Servier Agreement's inception and, during 2020, selected two additional hematological cancer targets beyond CD19 and two new solid tumor targets. With the addition of these new targets, we received development milestone payments in 2020 and may be eligible

to receive additional development milestone payments in 2021. Upon selection of an antigen target, we perform early-stage research and development on individual T cell modifications for the selected target, develop the resulting therapeutic product candidates through Phase 1 clinical trials and manufacture clinical trial material for use in Phase 2 clinical trials.

We received an upfront payment of $105.0 million under the Servier Agreement in 2016. At Phase 2 readiness for any product candidate covered by the Servier Agreement, Servier may exercise a commercial option to proceed with development and commercialization of the product candidate. Following the exercise of any such commercial option, Servier must use commercially reasonable efforts to develop and commercialize the product candidate. We have the ability to receive total payments, including the upfront payment, option fees and milestone payments, in the aggregate across all five targets of up to approximately $1.4 billion. This includes up to $1.3 billion in milestone payments, consisting of up to $329.3 million in development milestone payments and up to $925.0 million in commercial milestone payments. We are also entitled to receive tiered royalties ranging from the mid-single digit percentages to sub-teen percentages on worldwide net sales of any products developed under the Servier Agreement, subject to customary potential reductions. Servier's obligation to pay royalties to us expires on a country-by-country and licensed product-by-licensed product basis upon the latest of (1) the expiration of the last to expire valid claim of all Precision patents covering a licensed product, (2) expiration of all regulatory exclusivity with respect to a licensed product in the applicable country of sale, and (3) the expiration of 10 years following the first commercial sale of such licensed product in such country. We also have the right to participate in the development and commercialization of any licensed products resulting from the collaboration through a 50/50 co-development and co-promotion option in the United States, subject to our payment of an option fee, which is exercisable after Servier's commercial option exercise. So long as Servier holds a commercial license with respect to any particular licensed product, we may not develop, manufacture or commercialize any engineered human CAR T cells for use in humans directed to the same antigen target as the target of that licensed product.

Unless terminated earlier, the Servier Agreement expires upon the first to occur of (1) the expiration of the period in which Servier may nominate antigen targets, if there are no included targets under the agreement, (2) the expiration of the period in which Servier may exercise a commercial option on a licensed product candidate, if no commercial options have been exercised by Servier, or (3) the expiration of the last to expire royalty term for the licensed products and satisfaction of all of Servier's payment obligations under the agreement. Servier has the right to terminate the agreement for convenience, either in its entirety or on a target-by-target or product-by-product basis, by providing advance notice to us. We may terminate immediately upon notice to Servier if Servier (itself or through the use of certain affiliates or a third party) or any sublicensee initiates or participates in a patent challenge against our patents licensed by Servier under the agreement. In addition, the Servier Agreement may be terminated (a) by either party for the other party's material breach that remains uncured as specified in the agreement, (b) by either party upon the occurrence of certain insolvency-related events of the other party and (c) upon mutual agreement of the parties in the event either party suffers an event of force majeure as specified in the agreement. If Servier terminates the agreement for our uncured material breach of provisions in the agreement that restrict development, manufacture or commercialization of engineered human T cells with chimeric antigen receptors for use in humans directed to a target selected by Servier, certain licenses we grant to Servier will become royalty-free, fully paid-up, perpetual and irrevocable with respect to the licensed product candidates and licensed products directed to the target that was the subject of such breach, and Servier will be deemed to have previously exercised its commercial option for any then-existing licensed product candidates directed to such target.

Gilead

On July 6, 2020, Gilead Sciences ("Gilead") notified us of its termination of the collaboration and license agreement dated September 10, 2018, subsequently amended by Amendment No. 1 dated March 10, 2020 or (the "Gilead Agreement"), to develop genome editing tools using ARCUS to target viral DNA associated with the hepatitis B virus. Pursuant to the termination notice, the Gilead Agreement terminated on September 4, 2020. Upon termination, we regained full rights and all data we generated for the *in vivo* chronic hepatitis B program developed under the Gilead Agreement.

Duke University

In April 2006, we entered into the Duke License, pursuant to which Duke University ("Duke") granted us an exclusive (subject to certain non-commercial rights reserved by Duke), sublicensable, worldwide license under certain patents related to certain meganucleases and methods of making such meganucleases owned by Duke to develop, manufacture, use and commercialize products and processes that are covered by such patents, in all fields and in all applications. The patents that we license pursuant to the Duke License have been generated through the use of U.S. government funding and are therefore subject to certain federal regulations. See Part I, Item 1A. "Risk Factors— Risks Related to Intellectual Property—Some of our in-licensed intellectual property has been discovered through government funded programs and thus may be subject to federal regulations such as "march-in" rights, certain reporting requirements and a preference for U.S.-based companies, and compliance with such regulations may limit our exclusive rights and limit our ability to contract with non-U.S. manufacturers."

Under the Duke License, in addition to upfront licensing fees, we are also required to pay Duke (1) a total of $0.3 million in milestone payments, a portion of which we paid upon the completion of our Series A financing, a further portion of which we paid upon our first signed partnership in excess of $1 million, and the remainder of which we will be required to pay upon successful commercialization of seed traits and human therapeutics, (2) royalties in the low single digit percentages on net sales of licensed products and licensed processes sold by us and our affiliates, subject to certain reductions in certain circumstances, with certain annual minimum royalties, and (3) certain percentages of sublicensing revenue received under sublicenses granted to third parties, which are creditable against annual minimum royalties and are subject to certain reductions in certain circumstances. For sublicenses of non-commercial products, the percentage of sublicensing revenue payable to Duke is in the mid-teen percentages for sublicense revenues owed from royalties received and low double-digits for sublicense revenues owed from non-royalty payments. For sublicenses of commercial products created by us and derivatives thereof, the percentage is determined by the highest negotiated royalty rate in such sublicense. If the highest negotiated royalty rate between us and our sublicensee exceeds a mid-single digit percentage, the percentage of sublicensing revenue payable to Duke will be high single digit, decreasing to low single digit as the highest negotiated royalty rate in such sublicense increases.

We closed the transactions under the Lilly Agreement on January 6, 2021 following receipt of clearance under the Hart-Scott-Rodino Antitrust Improvements Act of 1976, as amended, and, as a result we are required to make $3.0 million in payments under the Duke License in 2021, net of any outstanding credits. See Note 14 to our audited consolidated financial statements included elsewhere in this Annual Report on Form 10-K for additional information regarding the Lilly Agreement.

The Duke License will expire upon the expiration of the last-to-expire patent that is licensed to us. We may terminate the Duke License by providing advance written notice as specified in the Duke License. Either party may terminate the Duke License in the event of the other party's uncured material breach or for the other party's fraud, willful misconduct or illegal conduct with respect to the subject matter of the Duke License.

Cellectis S.A.

In January 2014, we entered into a cross-license agreement with Cellectis S.A., which we refer to as the Cellectis License, in connection with a settlement of litigation matters (1) between Cellectis and us and (2) among Cellectis, Duke and us. Cellectis granted us a non-exclusive, sublicensable, worldwide, fully paid, royalty-free license to certain modified I-CreI homing endonuclease patents and Cellectis patents asserted in the litigation, to make, use and commercialize modified I-CreI homing nucleases and products developed using such nucleases, in all fields. The license we received from Cellectis is subject to the rights of a preexisting license agreement that Cellectis entered into with a third party, and the license granted to us excludes any rights exclusively granted by Cellectis under such preexisting license, which preexisting license is limited to certain specific applications unrelated to the fields of human therapeutics and plant agriculture, for so long as the rights under the preexisting license remain exclusive.

We granted Cellectis a non-exclusive, sublicensable, worldwide, fully paid-up, royalty-free license to certain modified I CreI homing endonuclease patents and our patents asserted in the litigation matters (1) between Cellectis and us and (2) among Cellectis, Duke and us to make, use and commercialize modified I-CreI homing nucleases and products developing using such nucleases, in all fields except those for which we did not receive rights from Cellectis due to the preexisting license.

The Cellectis License will expire upon the expiration of the last-to-expire valid claim of all of the patents licensed to or from each of the parties to the agreement. Either party may terminate any of the licenses granted under the agreement (1) in the event of the other party's material breach, subject to an opportunity to cure within the time period specified in the Cellectis License, or (2) if the other party directly or indirectly challenges a patent licensed to it by the other party.

Competition

As a diversified life sciences company, we compete in multiple different fields. The biotechnology, pharmaceutical and agricultural biotechnology industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on intellectual property and proprietary products. We principally compete with others developing and utilizing genome editing technology in the human health and plant sciences sectors, including companies such as Allogene Therapeutics, Inc., Alnylam Pharmaceuticals, Inc., Caribou Biosciences, Inc., Cellectis S.A., CRISPR Therapeutics, AG, Dicerna Pharmaceuticals, Inc., Editas Medicine, Inc., Intellia Therapeutics, Inc., Sangamo Therapeutics, Inc., and Beam Therapeutics, Inc.

We compete with many biotechnology and pharmaceutical companies, academic research institutions, governmental agencies and public and private research institutions. We expect that our operations focused on CAR T cell product candidate development and commercialization will face substantial competition from those focusing on immunotherapy solutions. Several companies, including Novartis Pharmaceuticals Corp. and Gilead have obtained FDA approval for autologous cell therapies, and a number of companies, including Cellectis S.A., Celgene Corp., Allogene Therapeutics and CRISPR Therapeutics AG, are pursuing allogeneic cell therapies. We expect that our operations focused on developing products for *in vivo* treatment of genetic disease will face substantial competition from others focusing on gene therapy treatments, especially those that may focus on conditions that our product candidates target. Moreover, any human therapeutics products that we may develop will compete with existing standards of care for the diseases and conditions that our product candidates target and other types of treatments, such as small molecule, antibody or protein therapies.

Many of our current or potential competitors in the therapeutics space, either alone or with their collaboration partners, have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials and marketing approved products than we do. In addition to competing on the bases of safety, efficacy, timing of development and commercialization, convenience, cost, availability of reimbursement and rate of adoption of potential product candidates, we may also compete with these competitors in recruiting and retaining qualified personnel, establishing clinical sites, establishing relationships with collaborators or other third parties, registering patients for clinical trials and acquiring technologies complementary to, or necessary for, our product development platforms. 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. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market.

Many of our current or potential competitors in the agricultural biotechnology space, either alone or with others, have significantly greater financial resources and expertise in research and development, manufacturing, testing and marketing approved products than we do. Mergers and acquisitions in the plant science, specialty food ingredient and agricultural biotechnology, seed and chemical 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 strategic relationships with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel, as well as in acquiring technologies complementary to, or necessary for, our food platform.

Furthermore, we rely upon a combination of patents and trade secret protection, as well as license and confidentiality agreements to protect the intellectual property related to our proprietary technologies, product candidate development programs and product candidates. Our success depends in large part on our ability to secure and maintain patent protection in the United States and other countries with respect to the ARCUS nucleases used in our existing allogeneic CAR T immunotherapy, *in vivo* gene correction and food programs, as well as any future product candidates. Moreover, the industries in which we operate are characterized by the existence of large numbers of patents and frequent allegations of patent infringement. If, therefore, we are unable to obtain and maintain patent protection for our technology and product candidates, or if the scope of the patent protection obtained or in-licensed is not sufficiently broad or if the validity of such patent protection is threatened, we may not be able to compete effectively, as it could create opportunities for competitors to enter the market or dissuade other companies from collaborating with us to develop products and technology, any of which would hurt our competitive position and could impair our ability to successfully commercialize our product candidates in any indication for which they are approved.

Intellectual property

Our success depends in part on our abilities to (1) obtain and maintain proprietary protection for ARCUS, (2) defend and enforce our intellectual property rights, in particular, our patent rights, (3) preserve the confidentiality of our know-how and trade secrets, and (4) operate without infringing valid and enforceable intellectual property rights of others. We seek to protect our proprietary position by, among other things, exclusively licensing U.S. and certain foreign patent applications, and filing U.S. and certain foreign patent applications related to ARCUS, existing and planned programs, and improvements that are important to the development of our business. We also rely on trademarks, trade secrets, know-how, continuing technological innovation and confidential information, and the pursuit of licensing opportunities, to develop and maintain our proprietary position and protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection. We seek to protect our proprietary technology and processes, in part, by confidentiality agreements and invention assignment agreements with our employees, consultants, scientific advisors, contractors and others who may have access to proprietary information, under which they are bound to assign to us inventions made during the term of their employment or term of service. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems.

We cannot be sure that patents will be granted with respect to any patent applications we have licensed or filed or may license or file in the future, and we cannot be sure that any patents we have licensed or which have been granted to us, or patents that may be licensed or granted to us in the future, will not be challenged, invalidated or circumvented or that such patents will be commercially useful in protecting our technology. Moreover, trade secrets can be difficult to protect. While we have confidence in the measures we take to protect and preserve our trade secrets, such measures can be breached, and we may not have adequate remedies for any such breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors. For more information regarding the risks related to our intellectual property, see Part I, Item 1A. “Risk Factors—Risks Related to Intellectual Property.”

Our patent portfolio consists of a combination of issued patents and pending patent applications that are owned by us or licensed by us from third parties. As of December 31, 2020, we have an exclusive license from Duke under 12 issued U.S. patents and one pending U.S. patent application. In addition, as of December 31, 2020, we own 26 issued U.S. patents, 27 pending non-provisional U.S. patent applications, and 13 pending Patent Cooperation Treaty (“PCT”) international patent applications. We also exclusively license from Duke or own many corresponding patents and patent applications outside the United States, as described below. We intend to pursue, when possible, additional patent protection, including composition of matter, method of use and process claims, related to ARCUS. We also intend to obtain rights to existing delivery technologies through one or more licenses from third parties.

ARCUS Platform Patent Families

We license one patent family from Duke and own three patent families that are directed to the core technologies employed in our ARCUS platform for nuclease design. Thus, each of our product candidates is protected by one or more patents in these families.

The first family, licensed from Duke, includes 12 issued U.S. patents, nine issued European patents, three issued Japanese patents, and one issued patent in each of Australia and Canada. This family also includes pending patent applications in each of the United States, Europe, Canada, and two pending patent applications in Japan. Patents in this family include claims directed to (1) recombinant meganucleases having altered cleavage specificity, altered heterodimer formation, and/or altered DNA binding affinity, (2) methods for cleaving target recognition sites in DNA using such meganucleases, and (3) methods for producing genetically modified eukaryotic cells using such meganucleases. Patents in this family have a standard expiration date of October 18, 2026, subject to potential extensions.

The second family, which we own, includes four issued U.S. patents, three issued patents in Europe, two issued patents in Japan, and one issued patent in Australia. This family also includes two pending patent applications in the United States, and pending patent applications in each of Europe, Japan and Australia. Patents in this family include claims directed to (1) recombinant single-chain meganucleases, and (2) methods for producing isolated genetically modified eukaryotic cells using such meganucleases. Patents in this family have a standard expiration date of October 31, 2028, subject to potential extensions.

The third family, which we own, includes three issued patents in the United States, and two issued patents in each of Europe and Australia. This family also includes two pending patent applications in the United States and one pending patent application in Europe. Patents in this family include claims directed to methods of cleaving DNA at specific four base pair sites using a recombinant meganuclease. Patents in this family have a standard expiration date of July 14, 2029, subject to potential extensions.

The fourth family, which we own, includes a pending PCT international patent application. Patent applications in this family include claims directed to recombinant meganucleases engineered to cleave recognition sequences having specific four base pair sites. Patents in this family, if issued, will have a standard expiration date of May 7, 2040, subject to potential extensions.

Immunotherapy Patent Families

We own 19 patent families that are directed to immunotherapy, including CAR T cell therapies. Some of these are applicable to immunotherapies and/or CAR T cells directed to killing a variety of different types of infected or cancerous cells. Others are directed to specific indications in which cells expressing particular antigens are targeted, or methods of manufacturing immunotherapies. Each of our immunotherapy product candidates is protected by one or more patents in these families.

The first family includes nine issued U.S. patents, one issued patent in each of Europe and Japan, and pending patent applications in each of the United States, Europe, Australia, Canada, China, Hong Kong, Israel, Japan, Mexico and South Korea. Patents in this family include claims directed to (1) populations of genetically modified human T cells in which 20%-65% of the cells have reduced expression of an endogenous TCR and express an anti-cancer antigen CAR from DNA inserted into the cells' TCR alpha constant region (TRAC) gene, (2) methods for using such populations of genetically modified human T cells for cancer immunotherapy, (3) pharmaceutical compositions comprising such populations of genetically modified human T cells, (4) genetically modified human T cells which have reduced expression of an endogenous TCR and express an anti-cancer antigen CAR from DNA inserted into the cells' TRAC gene, (5) methods for using such genetically modified human T cells for cancer immunotherapy, and (6) pharmaceutical compositions comprising such genetically modified human T cells. Patents in this family have a standard expiration date of October 5, 2036, subject to potential extensions.

The second family includes one issued patent in each of the United States and Europe, pending patent applications in each of the United States, Europe, Hong Kong, Canada and Japan, and two pending patent applications in Australia. Patent applications in this family include claims directed to (1) first-generation recombinant meganucleases that cleave a target in the TRAC gene, (2) nucleic acids and vectors encoding such recombinant meganucleases, (3) methods for producing genetically modified eukaryotic cells, including CAR T cells, using such meganucleases, and (4) methods of using such genetically modified eukaryotic cells for cancer immunotherapy. Patents in this family will have a standard expiration date of October 5, 2036, subject to potential extensions.

The third family includes a pending PCT international patent application, and pending patent applications in each of the United States, Europe, Australia, Canada, China, Israel, Japan, Mexico, and South Korea. Patent applications in this family include claims directed to (1) second-generation engineered meganucleases that cleave a specific target in the TRAC gene, (2) nucleic acids and vectors encoding such recombinant meganucleases, (3) methods for producing genetically modified eukaryotic cells, including CAR T cells, using such meganucleases, (4) genetically modified eukaryotic cells or populations of cells prepared by such methods, (5) pharmaceutical compositions comprising such cells or populations of cells, and (6) methods of treating diseases using such cells, populations of cells or pharmaceutical compositions to treat diseases, including cancer immunotherapy. Patents in this family, if issued, will likely have a standard expiration date of April 11, 2039, subject to potential extensions.

The fourth family includes one issued patent in each of the United States and Europe, pending patent applications in Europe, Canada and Japan, and two pending patent applications in the United States and Australia. Patent applications in this family include claims directed to (1) nucleic acids encoding co-stimulatory domains having certain amino acid sequences, (2) recombinant DNA constructs and vectors comprising such nucleic acids, (3) nucleic acids and vectors encoding such recombinant meganucleases, (4) genetically modified cells comprising such nucleic acids, (5) methods for producing such genetically modified cells, (6) pharmaceutical compositions comprising such cells, and (7) methods of immunotherapy using such cells. Patents in this family have a standard expiration date of October 4, 2037, subject to potential extensions.

The fifth family includes pending patent applications in the United States and Europe. Patent applications in this family include claims directed to (1) methods of reducing cytotoxicity associated with DNA transfection in primary eukaryotic cells, (2) methods for increasing the number of gene-edited primary eukaryotic cells following DNA transfection, (3) methods for increasing gene editing frequency in primary eukaryotic cells following DNA transfection, (4) methods for increasing the number of primary eukaryotic cells comprising targeted insertion of an exogenous sequence of interest into the genome following DNA transfection, (5) methods for increasing insertion frequency of an exogenous sequence of interest into the genome in primary eukaryotic cells following DNA transfection, (6) methods for high throughput screening of primary human T cells expressing a CAR or exogenous TCR, (7) methods for high throughput screening of primary human T cells expressing a CAR or exogenous TCR, and (8) genetically modified primary eukaryotic cells produced by such methods. Patents in this family, if issued, will have a standard expiration date of April 30, 2038, subject to potential extensions.

The sixth family includes pending patent applications in Europe, Australia, Canada and Japan, and two pending patent applications in the United States. Patent applications in this family include claims directed to (1) recombinant meganucleases that recognize and cleave a recognition sequence within the human beta-2-microglobulin gene, (2) nucleic acids and vectors encoding such recombinant meganucleases, (3) methods for producing genetically modified eukaryotic cells, including CAR T cells, using such meganucleases, (4) populations of genetically modified eukaryotic cells in which 80% of the cells have reduced expression of an endogenous TCR and 80% of the cells have reduced expression of beta-2-microglobulin, (5) pharmaceutical compositions comprising such populations of

genetically modified eukaryotic cells, and (6) methods for using such genetically modified eukaryotic cells for cancer immunotherapy. Patents in this family, if issued, will have a standard expiration date of December 22, 2036, subject to potential extensions.

The seventh family includes an issued patent in the United States, and pending patent applications in the United States, Europe, Australia, Canada, Hong Kong, and Japan. Patent applications in this family include claims directed to (1) nucleic acids encoding an engineered antigen receptor (e.g., a CAR) and an inhibitory molecule (e.g., an RNA interfering with beta-2-microglobulin expression), (2) genetically modified eukaryotic cells comprising such nucleic acids, (3) methods for producing such genetically modified eukaryotic cells using such nucleic acids and an engineered nuclease that promotes insertion of such nucleic acids, (4) genetically modified eukaryotic cells expressing an engineered antigen receptor and having expression of beta-2-microglobulin or MHC Class I molecules reduced by 10%-95%, (5) pharmaceutical compositions comprising such genetically modified eukaryotic cells, and (6) methods for using such genetically modified eukaryotic cells for immunotherapy. Patents in this family have a standard expiration date of May 8, 2038, subject to potential extensions.

The eighth family includes pending patent applications in the United States, Europe, Australia, Canada, Hong Kong, and Japan. Patent applications in this family include claims directed to (1) engineered meganucleases that recognize and cleave a recognition sequence in an upstream intron of the human TRAC gene, (2) nucleic acids and vectors encoding such engineered meganucleases, (3) methods for producing genetically modified T cells using such nucleic acids or vectors, (4) genetically modified T cells in which an exogenous sequence is inserted into an upstream intron of the human TRAC gene and endogenous TCR expression is reduced, (5) populations of such genetically modified T cells, (6) pharmaceutical compositions comprising such genetically modified T cells, and (7) methods of treating disease using such genetically modified T cells and pharmaceutical compositions, including cancer immunotherapy. Patents in this family, if issued, will have a standard expiration date of June 27, 2038, subject to potential extensions.

The ninth family includes pending patent applications in the United States and Europe. Patent applications in this family include claims directed to (1) nucleic acids and vectors encoding certain modified human epidermal growth factor receptor, or EGFRs, (2) genetically modified cells and populations of cells, including T cells and CAR T cells, expressing such modified EGFRs, (3) methods for producing such genetically modified cells using such nucleic acids or vectors encoding such modified EGFRs, (4) pharmaceutical compositions comprising such genetically modified cells, (5) methods for isolating such genetically modified cells, (6) methods of treating disease using such genetically modified cells and pharmaceutical compositions, including cancer immunotherapy, and (7) methods of depleting such genetically modified cells in a subject using anti-modified EGFR antibodies. Patents in this family, if issued, will likely have a standard expiration date of October 3, 2038, subject to potential extensions.

The tenth family includes a pending provisional patent application in the United States and a pending PCT international patent application. Patent applications in this family include claims directed to (1) methods for preparing genetically-modified immune cells, (2) populations of genetically-modified immune cells, (3) pharmaceutical compositions comprising such populations of genetically-modified immune cells, (4) methods of treating a disease using such populations of genetically-modified immune cells, (5) lipid nanoparticle compositions, and (6) kits for transfecting a eukaryotic cell with mRNA. Patents in this family, if issued, will have a standard expiration date of April 3, 2040, subject to potential extensions.

The eleventh family includes a pending provisional patent application in the United States, a pending PCT international patent application, and a pending non-provisional patent application in the United States. Patent applications in this family include claims directed to (1) a genetically-modified immune cell comprising in its genome a nucleic acid sequence encoding a microRNA-adapted shRNA, (2) a method for reducing the expression of an endogenous protein in an immune cell, (3) immune cells made by such methods, (4) populations of such immune cells, (5) pharmaceutical compositions comprising such populations of immune cells, and (6) methods of immunotherapy for treating a disease in a subject. Patents in this family, if issued, will have a standard expiration date of April 3, 2040, subject to potential extensions.

We own eight additional patent families that include pending provisional patent applications in the United States or pending PCT international patent applications that are directed to immunotherapies, including CAR T cell therapies, or to technologies that are useful for the manufacture of immunotherapies. We jointly own one patent family that includes a pending PCT international patent application directed to immunotherapies. We will determine in the future whether to pursue each of these applications.

In October 2020, we announced the U.S. Patent and Trademark Office's PTAB issued judgements in our favor in two patent interference proceedings that challenged nine U.S. patents we owned. The patents, which issued in 2018, relate to allogeneic CAR T cells produced by inserting a gene encoding a CAR into the TRAC locus, as well as methods of using those cells for cancer immunotherapy. In the interference proceedings, a third party argued that it had invented the technology in 2012. The PTAB,

however, found that the third-party patent application did not satisfy the written description requirement and rejected these claims while maintaining the claims in all nine of our patents.

Other Patent Families

We own three patent families directed to gene therapy for Hepatitis B virus. The first family includes two issued patents in the United States, one issued patent in Japan, and pending patent applications in the United States, Europe, Japan, Canada, Australia, China, South Korea, Mexico, Israel, Colombia, Costa Rica, the Dominican Republic, Egypt, Eurasia, Guatemala, Hong Kong, Morocco, Malaysia, New Zealand, Nigeria, Panama, Peru, the Philippines, Saudi Arabia, South Africa, Thailand and Vietnam. Patents in this family will have a standard expiration date of October 13, 2037, subject to potential extensions. The second family includes a pending PCT international patent application and patent applications in the United States, Europe, Taiwan and the Gulf Cooperation Council. Patents in this family, if issued, will have a standard expiration date of April 11, 2039, or April 12, 2039, subject to potential extensions. The third family includes a pending PCT international patent application. Patents in this family, if issued, will have a standard expiration date of December 4, 2040, subject to potential extensions.

We own one patent family directed to engineered meganucleases and methods of treatment targeting the PCSK9 gene, which is associated with familial hypercholesterolemia. This family includes pending patent applications in the United States, Europe, Australia, Canada, China, Hong Kong, Israel, Japan, Mexico, and South Korea. Patents in this family, if issued, will have a standard expiration date of April 20, 2038, subject to potential extensions.

We own two patent families directed to engineered meganucleases and methods of treatment targeting the rhodopsin gene, which is associated with retinitis pigmentosa. The first family includes two issued patents in the United States, one issued patent in Japan, pending patent applications in the United States, Europe, Canada and Japan, and two pending patent applications in Australia. Patents in this family will have a standard expiration date of September 8, 2036, subject to potential extensions. The second family includes two pending provisional patent application in the United States. Patents in this family, if issued, will likely have a standard expiration date of May 12, 2041, subject to potential extensions.

We own one patent family that is directed to engineered meganucleases and methods of treatment targeting the hydroxyacid oxidase 1 gene, which is associated with primary hyperoxaluria 1. This family includes a pending PCT international patent application. Patents in this family, if issued, will have a standard expiration date of December 20, 2039, subject to potential extensions.

We own two patent families that are directed to engineered meganucleases and methods of treatment targeting the Factor VIII gene, which is associated with Hemophilia A. The first family includes pending patent applications in the United States, Europe, Australia, Canada, and Japan. Patents in this family, if issued, will have a standard expiration date of May 3, 2037, subject to potential extensions. The second family includes pending patent applications in the United States and Europe. Patents in this family, if issued, will have a standard expiration date of November 1, 2038, subject to potential extensions.

We own one patent family directed to engineered meganucleases and methods of treatment targeting the ApoC3 gene, which is associated with diseases resulting from abnormal triglyceride synthesis. This family includes a pending provisional patent application in the United States. Patents in this family, if issued, will likely have a standard expiration date of August 11, 2041, subject to potential extensions.

We own one patent family directed to engineered meganucleases and methods of treatment targeting the transthyretin (TTR) gene, which is associated with TTR amyloidosis. This family includes a pending provisional patent applications in the United States. Patents in this family, if issued, will likely have a standard expiration date of August 21, 2041, subject to potential extensions.

We own two patent families directed to engineered meganucleases and methods of treatment targeting the dystrophin gene, which is associated with Duchenne Muscular Dystrophy. The first family includes an issued patent in Europe, pending patent applications in Europe, Australia, Canada and Japan, and two pending patent applications in the United States. Patents in this family will have a standard expiration date of March 12, 2035, subject to potential extensions. The second family includes a pending provisional patent application in the United States. Patent applications in this family, if issued, will likely have a standard expiration date of November 12, 2041.

We own one patent family directed to engineered meganucleases and methods of treatment targeting genomic trinucleotide repeats, which are associated with several trinucleotide repeat disorders. This family includes pending patent applications in the United States and Europe. Patents in this family, if issued, will have a standard expiration date of May 2, 2036, subject to potential extensions.

We license from Duke one patent family directed to engineered fusion proteins comprising engineered meganuclease domains and effector domains which may be useful in controlling gene expression. This patent family includes two pending patent applications in

the United States. Patents in this family, if issued, will have a standard expiration date of October 18, 2026, subject to potential extensions.

We own one patent family directed to engineered meganucleases that target amplifiable genetic loci and may be useful in producing cells with amplified transgenes. This family includes two issued patents in Europe, one issued patent in the United States, and one pending patent application in each of the United States and Europe. Patents in this family will have a standard expiration date of June 1, 2032, subject to potential extensions.

We own two patent families directed to self-limiting viral vectors (e.g., AAV vectors) that encode engineered meganucleases which eliminate the vector after gene delivery. The first family includes an issued patent in the United States, and pending patent applications in the United States and Europe. Patents in this family will have a standard expiration date of June 20, 2036, subject to potential extensions. The second family includes one pending provisional patent application in the United States. Patents in this family, if issued, will likely have a standard expiration date of May 11, 2041, subject to potential extensions.

We own one patent family directed to compositions and methods for sequential stacking of nucleic acid sequences into a genomic locus. This family includes a pending PCT international patent application. Patents in this family, if issued, will have a standard expiration date of July 24, 2040, subject to potential extensions.

We own one patent family directed to eukaryotic cells comprising a modified transferrin gene that includes an exogenous nucleic acid sequence encoding a polypeptide of interest. This family includes a pending PCT international patent application. Patents in this family, if issued, will have a standard expiration date of January 10, 2040.

We own one patent family directed to methods for separation of empty and full AAV capsids during manufacturing. This family includes a pending provisional application in the United States. Patents in this family, if issued, will likely have a standard expiration date of February 6, 2041.

We own an issued patent in the United States directed to engineered meganucleases which target a genetic locus in maize and methods for genetically modifying that locus in maize. That patent has a standard expiration date of March 2, 2029, subject to potential extensions.

We own, through our Elo Life Systems subsidiary, one patent family directed to the modulation of endogenous mogroside pathway genes in watermelon and other cucurbits. This family includes a pending provisional patent application in the United States. Patents in this family, if issued, will likely have a standard expiration date of March 31, 2041, subject to potential extensions.

We own, through our Elo Life Systems subsidiary, one patent family directed to methods for producing vanilla plants with improved flavor and agronomic product. This family includes a pending provisional patent application in the United States. Patents in this family, if issued, will likely have a standard expiration date of October 23, 2041, subject to potential extensions.

For any individual patent, the term depends on the applicable law in the country in which the patent is granted. In most countries where we have filed patent applications or in-licensed patents and patent applications, patents have a term of 20 years from the application filing date or earliest claimed non-provisional priority date. In the United States, the patent term is 20 years but may be shortened if a patent is terminally disclaimed over another patent that expires earlier. The term of a U.S. patent may also be lengthened by a patent term adjustment to address administrative delays by the USPTO in granting a patent.

In the United States, the term of a patent that covers an FDA-approved drug or biologic may be eligible for patent term extension in order to restore the period of a patent term lost during the premarket FDA regulatory review process. The Hatch-Waxman Act permits a patent term extension of up to five years beyond the natural expiration of the patent. The patent term restoration period is generally equal to the portion of the FDA regulatory review period for the approved product that occurs after the date the patent issued, subject to certain exceptions. Only one patent may be extended for a regulatory review period for any product, and the application for the extension must be submitted prior to the expiration of the patent. In the future, we may decide to apply for restoration of patent term for one of our currently owned or licensed patents to extend its current expiration date, depending on the expected length of the clinical studies and other factors involved in the filing of the relevant BLA.

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 or other intellectual property as an inventor or co-inventor. If we are required to and unable to obtain an exclusive license to any such third-party co-owners' interest in such patent applications, such co-owners may be able to license their rights to other third parties, including our competitors. In addition, we may need the cooperation of any such co-owners to enforce any patents that issue from such patent applications against third parties, and such cooperation may not be provided to us. We or our licensors are subject to and may also become a party to similar proceedings or priority disputes in Europe or other foreign jurisdictions.

Our registered trademark portfolio currently contains four registered trademarks in the United States, including ARCUS, ARC nuclease, Elo Life Systems and Zeromelon. We also own registered trademarks for both ARCUS and ARC nuclease in Europe, China and Australia, and a registered trademark for ARCUS in Canada. We own a registered trademark for Elo Life Systems in Australia, and pending trademark application for Zeromelon in each of Australia, Brazil, Canada, China, Europe, Germany, India, Japan, Mexico, South Korea, and the United Kingdom. Additionally, we own pending trademark applications for Zerocanola, Precision Biotechnology and Climate-Smart in the United States, Australia, Brazil, Canada, China, Europe, Japan, and Mexico.

Licensed Intellectual Property

Duke University

In April 2006, we exclusively licensed from Duke families of patents and patent applications related to certain meganucleases and methods of making such nucleases owned by Duke. The patent family covered by the Duke License comprises the core patents covering ARCUS described above. See "—License and Collaboration Agreements—Duke University" above for additional information regarding the Duke License.

Cellectis S.A.

In January 2014, we entered into the Cellectis License, which relates to certain modified I-CreI homing endonuclease patents and patents that had been subject to litigation between us and Cellectis. The patents to which we have rights under the cross-license include at least eight issued patents in each of the United States and Australia, seven issued patents in Europe, two issued patents in Canada and one issued patent in Japan. These patents have standard expiration dates prior to January 29, 2034, subject to potential extensions. See "—License and Collaboration Agreements—Cellectis S.A." above for additional information regarding the Cellectis License.

Government Regulation

The FDA and other regulatory authorities at federal, state, and local levels, as well as in foreign countries, extensively regulate, among other things, the research, development, testing, manufacture, quality control, import, export, safety, effectiveness, labeling, packaging, storage, distribution, record keeping, approval, advertising, promotion, marketing, post-approval monitoring, and post-approval reporting of biological product candidates such as those we are developing. We, along with third-party contractors, will be required to navigate the various preclinical, clinical and commercial approval requirements of the governing regulatory agencies of the countries in which we wish to conduct studies or seek approval or licensure of our product candidates. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources.

U.S. Biologics Regulation

The process required by the FDA before biologic product candidates may be marketed in the United States generally involves the following:

- completion of preclinical laboratory tests and animal studies performed in accordance with the FDA's Good Laboratory Practice requirements, or GLPs;
- demonstration of successful, reproducible manufacture of clinical trial material produced in compliance with current Good Manufacturing Practices (cGMPs) and consistent with all release specifications for the product at initial manufacture and over time when stored under defined conditions;
- submission to the FDA of an IND, which must become effective before clinical trials may begin, and which must be properly maintained throughout the course of clinical development;
- approval by an Investigational Review Board ("IRB") or ethics committee, and additional scientific and biosafety review committees at each clinical site before the trial is commenced;
- performance of adequate and well-controlled human clinical trials following protocols agreed to by FDA to establish the safety, purity and potency of the proposed biologic product candidate for its intended purpose;
- preparation of and submission to the FDA of a BLA after completion of all pivotal clinical trials;
- a determination by the FDA within 60 days of its receipt of a BLA to file the application for review;

- satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities at which the proposed commercial product is produced to assess compliance with cGMP and to assure that the facilities, methods and controls are adequate to preserve the biological product's continued safety, purity and potency, and of selected clinical investigation sites to assess compliance with GCPs; and
- satisfactory completion of an FDA Advisory Committee review, if applicable;
- FDA review and approval of the BLA to permit commercial marketing of the product for particular indications for use in the United States.

Prior to beginning the first clinical trial with a product candidate in the United States, we must submit an IND to the FDA. An IND is a request for authorization from the FDA to administer an investigational new drug product to humans. A central focus of an IND submission is on the general investigational plan and the protocol(s) for clinical studies. The IND also includes results of animal and *in vitro* studies assessing the toxicology, pharmacokinetics, pharmacology, and pharmacodynamic characteristics of the product; chemistry, manufacturing, and controls information; and any available human data or literature to support the use of the investigational product according to the proposed clinical protocol including the proposed dose level(s). An IND must become effective before human clinical trials may begin. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, raises safety concerns or questions about the proposed clinical trial. In such a case, the IND may be placed on clinical hold and the IND sponsor and the FDA must resolve any outstanding concerns or questions before the clinical trial can begin. Submission of an IND therefore may or may not result in FDA authorization to begin a clinical trial.

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 of institutional biosafety committees, or IBCs, as set forth in the NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules, or NIH Guidelines. 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 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.

Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators in accordance with GCPs, which include the requirement that all research subjects provide their informed consent for their participation in any clinical study. Clinical trials are conducted under protocols detailing, among other things, the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. A separate submission to the existing IND must be made for each successive clinical trial conducted during product development and for any subsequent protocol amendments. Furthermore, for each site proposing to conduct the clinical trial an independent IRB must review and approve the plan for any clinical trial and the informed consent form before the clinical trial begins at that site, and must monitor the study until completed. Regulatory authorities, the IRB, or the sponsor may suspend a clinical trial at any time on various grounds, including a finding that the subjects are being exposed to an unacceptable health risk or that the trial is unlikely to meet its stated objectives. Some studies also include oversight by an independent group of qualified experts organized by the clinical study sponsor, known as a data safety monitoring board, which provides authorization for whether or not a study may move forward at designated check points based on access to certain data from the study and may halt the clinical trial if it determines that there is an unacceptable safety risk for subjects or other grounds, such as no demonstration of efficacy. There are also requirements governing the reporting of ongoing clinical studies and clinical study results to public registries.

For purposes of BLA approval, human clinical trials are typically conducted in three sequential phases that may overlap or be combined:

- Phase 1—The investigational product is initially introduced into healthy human subjects or patients with the target disease or condition. These studies are designed to test the safety, dosage tolerance, absorption, metabolism and distribution of the investigational product in humans, the side effects associated with increasing doses, and, if possible, to gain early evidence on effectiveness.
- Phase 2—The investigational product is administered to a limited patient population with a specified disease or condition to evaluate the preliminary efficacy, optimal dosages and dosing schedule and to identify possible adverse side effects and safety risks. Multiple Phase 2 clinical trials may be conducted to obtain information prior to beginning larger and more expensive Phase 3 clinical trials.

- Phase 3—The investigational product is administered to an expanded patient population to further evaluate dosage, to provide statistically significant evidence of clinical efficacy and to further test for safety, generally at multiple geographically dispersed clinical trial sites. These clinical trials are intended to establish the overall risk/benefit ratio of the investigational product and to provide an adequate basis for product approval.
- Phase 4—In some cases, the FDA may require, or companies may voluntarily pursue, additional clinical trials after a product is approved to gain more information about the product. These so-called Phase 4 studies may be made a condition to approval of the BLA.

Concurrent with clinical trials, companies may complete additional animal studies and develop additional information about the biological characteristics of the product candidate, and must finalize a process for manufacturing the product in commercial quantities in accordance with cGMP. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, must develop methods for testing the identity, strength, quality and purity of the final product, or for biologics, the safety, purity and potency. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life.

BLA Submission and Review by the FDA

Assuming successful completion of all required testing in accordance with all applicable regulatory requirements, the results of product development, nonclinical studies and clinical trials are submitted to the FDA as part of a BLA requesting approval to market the product for one or more indications. The BLA must include all relevant data available from pertinent preclinical and clinical studies, including negative or ambiguous results as well as positive findings, together with detailed information relating to the product's chemistry, manufacturing, controls, and proposed labeling, among other things. Data can come from company-sponsored clinical studies intended to test the safety and effectiveness of a use of the product, or from a number of alternative sources, including studies initiated by investigators. The submission of a BLA requires payment of a substantial user fee to FDA, and the sponsor of an approved BLA is also subject to an annual program fee. These fees are typically increased annually. A waiver of user fees may be obtained under certain limited circumstances. Additionally, no user fees are assessed on BLAs for products designated as orphan drugs, unless the application also includes a non-orphan indication.

Once a BLA has been submitted, the FDA's goal is to review standard applications within ten months after it accepts the application for filing, or, if the application qualifies for priority review, six months after the FDA accepts the application for filing. Priority review designation will direct overall attention and resources to the evaluation of applications for products that, if approved, would be significant improvements in the safety or effectiveness of the treatment, diagnosis, or prevention of serious conditions. In both standard and priority reviews, the review process is often significantly extended by FDA requests for additional information or clarification. The FDA reviews a BLA to determine, among other things, whether a product is safe, pure and potent and the facility in which it is manufactured, processed, packed, or held meets standards designed to assure the product's continued safety, purity and potency. The FDA may convene an advisory committee to provide clinical insight on application review questions. Before approving a BLA, the FDA will typically inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP and adequate to assure consistent production of the product within required specifications. Additionally, before approving a BLA, the FDA will typically inspect one or more clinical sites involved in the pivotal studies submitted in the BLA to assure compliance with GCP.

After the FDA evaluates a BLA and conducts inspections of manufacturing facilities where the investigational product and/or its drug substance will be produced, the FDA may issue an approval letter or a Complete Response Letter ("CRL") if the FDA determines that the application, manufacturing process or manufacturing facilities are not acceptable. In the CRL, the FDA will outline the deficiencies in the BLA submission and often will request additional information or testing that the applicant might perform to place the BLA in condition for approval, including requests for additional information or clarification. Notwithstanding the submission of any requested additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. Note that where the FDA determines that the data supporting the application are inadequate to support approval, the FDA may issue the CRL without first conducting required inspections, testing submitted product lots, and/or reviewing proposed labeling. The FDA may delay or refuse approval of a BLA if applicable regulatory criteria are not satisfied, require additional testing or information and/or require post-marketing testing and surveillance to monitor safety or efficacy of a product.

If regulatory approval of a product is granted, such approval will be granted for particular indications and may entail limitations on the indicated uses for which such product may be marketed. For example, the FDA may approve the BLA with the requirement that a Risk Evaluation and Mitigation Strategy ("REMS") be established to ensure the benefits of the product outweigh its risks when used according to the approved label. A REMS is a safety strategy to manage a known or potential serious risk associated with a medicine and to enable patients to have continued access to such medicines by managing their safe use, and could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries, required prescriber training, and other risk minimization tools. The FDA also may condition approval on, among other things, changes to

proposed labeling or the development of adequate controls and specifications. Once approved, the FDA may withdraw the product approval if compliance with pre- and post-marketing requirements is not maintained or if problems occur after the product reaches the marketplace. The FDA may require one or more Phase IV post-market studies and surveillance to further assess and monitor the product's safety and effectiveness after commercialization, and may limit further marketing of the product based on the results of these post-marketing studies. In addition, new government requirements, including those resulting from new legislation, may be established, or the FDA's policies may change, which could impact the timeline for regulatory approval or otherwise impact ongoing development programs.

Expedited Development and Review Programs

A sponsor may seek approval of its product candidate under programs designed to accelerate FDA's review and approval of new drugs and biological products that meet certain criteria. Specifically, new drugs and biological products are eligible for fast track designation if they are intended to treat a serious or life-threatening disease or condition and demonstrate the potential to address unmet medical needs for the disease or condition. For a fast track product, the FDA may consider sections of the 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. A fast track designated product candidate may also qualify for priority review, under which the FDA sets the target date for FDA action on the BLA at six months after the FDA accepts the application for filing. Priority review is granted pending availability of FDA review resources for the expedited review and when there is evidence that the proposed product would be a significant improvement in the safety or effectiveness of the treatment, diagnosis, or prevention of a serious disease or condition. If criteria are not met for priority review, the application is subject to the standard FDA review period of 10 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 accelerated approval program, the FDA may approve a BLA on the basis of either a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. Post-marketing studies or completion of ongoing studies after marketing approval are generally required to verify the biologic's clinical benefit in relationship to the surrogate endpoint or ultimate outcome in relationship to the clinical benefit. In addition, the FDA currently requires as a condition for accelerated approval pre-approval of promotional materials, which could adversely impact the timing of the commercial launch of the product. FDA may 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.

In addition, the Food and Drug Administration Safety and Innovation Act, or the FDASIA, which was enacted and signed into law in 2012, established the breakthrough therapy designation. A sponsor may seek FDA designation of its product candidate as a breakthrough therapy if the product candidate is intended, alone or in combination with one or more other drugs or biologics, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the therapy may demonstrate substantial improvement over existing 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 will gather the nonclinical and clinical data necessary for approval as efficiently 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.

The Regenerative Medicine Advanced Therapy, or RMAT, designation facilitates an efficient development program for, and expedites review of, any drug that meets the following criteria: (1) 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; (2) it is intended to treat, modify, reverse, or cure a serious or life-threatening disease or condition; and (3) 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 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 studies, 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.

Fast track designation, priority review, breakthrough therapy designation and RMAT designation do not change the standards for approval but may expedite the development or approval process. 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 decide that the time period for FDA review or approval will not be shortened.

Orphan Drug Designation and Exclusivity

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug or biologic intended to treat a rare disease or condition, defined as a disease or condition with a patient population of fewer than 200,000 individuals in the United States, or a patient population greater than 200,000 individuals in the United States and when there is no reasonable expectation that the cost of developing and making available the drug or biologic in the United States will be recovered from sales in the United States for that drug or biologic. Orphan drug designation must be requested before submitting a BLA. After the FDA grants orphan drug designation, the generic identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA.

If a product that has orphan drug designation subsequently receives the first FDA approval for a particular active ingredient within the 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 a full BLA, to market the same active ingredient 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. Orphan drug exclusivity does not prevent the FDA from approving a different drug or biologic for the same disease or condition, or the same drug or biologic for a different disease or condition. Among the other benefits of orphan drug designation are tax credits for certain research and a waiver of the BLA application user fee.

A designated orphan drug many not receive orphan drug exclusivity if it is approved for a use that is broader than the indication for which it received orphan designation. In addition, orphan drug exclusive marketing rights in the United States may be lost if the FDA later determines that the request for designation was materially defective or, as noted above, if the second applicant demonstrates that its product is clinically superior to the approved product with orphan exclusivity or the manufacturer of the approved product is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition. We plan to seek orphan drug designation for some or all of our product candidates in specific orphan indications in which there is a medically plausible basis for the use of these products.

Post-Approval Requirements

Any products manufactured or distributed by us pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to record-keeping, reporting of adverse experiences, periodic reporting, product sampling and distribution, and advertising and promotion of the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA review and approval. There also are continuing, annual program fees for any marketed products. Biologic manufacturers and their subcontractors 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, which impose certain procedural and documentation requirements upon us and our third-party manufacturers. Changes to the manufacturing process are strictly regulated, and, depending on the significance of the change, may require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting requirements upon us and any third-party manufacturers that we may decide to use. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain compliance with cGMP and other aspects of regulatory compliance.

The FDA may withdraw approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical studies to assess new safety risks; or imposition of distribution restrictions or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical studies;
- refusal of the FDA to approve pending applications or supplements to approved applications, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products;
- consent decrees, corporate integrity agreements, debarment or exclusion from federal healthcare programs;
- mandated modification of promotional materials and labeling and the issuance of corrective information;
- the issuance of safety alerts, Dear Healthcare Provider letters, press releases and other communications containing warnings or other safety information about the product; or
- injunctions or the imposition of civil or criminal penalties.

The FDA closely regulates the marketing, labeling, advertising and promotion of biologics. A company can make only those claims relating to safety and efficacy, purity and potency that are approved by the FDA and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses. Failure to comply with these requirements can result in, among other things, adverse publicity, warning letters, corrective advertising and potential civil and criminal penalties. Physicians may prescribe legally available products for uses that are not described in the product's labeling and that differ from those tested by us and approved by the FDA. Such off-label uses are common across medical specialties. Physicians may believe that such off-label uses are the best treatment for many patients in varied circumstances. The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, restrict manufacturer's communications on the subject of off-label use of their products.

Biosimilars and Exclusivity

The Affordable Care Act, signed into law in 2010, includes a subtitle called the BPCIA, which created an abbreviated approval pathway for biological products that are biosimilar to or interchangeable with an FDA-licensed reference biological product. The FDA has issued several guidance documents outlining an approach to review and approval of biosimilars.

Biosimilarity, which requires that there be no clinically meaningful differences between the biological product and the reference product in terms of safety, purity, and potency, can be shown through analytical studies, animal studies, and a clinical study or studies. Interchangeability requires that a product is biosimilar to the reference product and the product must demonstrate that it can be expected to produce the same clinical results as the reference product in any given patient and, for products that are administered multiple times to an individual, the biologic and the reference biologic 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 biologic. However, complexities associated with the larger, and often more complex, structures of biological products, as well as the processes by which such products are manufactured, pose significant hurdles to implementation of the abbreviated approval pathway that are still being worked out by the FDA.

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 full BLA for the competing product containing that applicant's own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of its product. The BPCIA also created certain exclusivity periods for biosimilars approved as interchangeable products. At this juncture, it is unclear whether products deemed "interchangeable" by the FDA will, in fact, be readily substituted by pharmacies, which are governed by state pharmacy law.

A biological 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.

The BPCIA is complex and continues to be interpreted and implemented by the FDA. In addition, government proposals have sought to reduce the 12-year reference product exclusivity period. Other aspects of the BPCIA, some of which may impact the BPCIA exclusivity provisions, have also been the subject of recent litigation. As a result, the ultimate impact, implementation, and impact of the BPCIA is subject to significant uncertainty.

Genetically Engineered Food Products

In the United States, the FDA and the USDA are primarily responsible for overseeing food regulation and safety, although many other federal agencies also play a role in food regulation.

USDA has jurisdiction over certain genetically engineered crops through the Animal and Plant Health Inspection Services, or APHIS. Under the Plant Protection Act and APHIS' Part 340 regulations, USDA requires anyone who wishes to import, transport interstate, or release into the environment a "regulated article" to apply for a permit or, in some cases, notify APHIS that the introduction will be made. Regulated articles are defined as "any organism which has been altered or produced through genetic engineering which USDA determines is a plant pest or has reason to believe is a plant pest." Regulated articles may be subject to extensive regulation, including both permitting requirements and inspections. However, to the extent products are subject to APHIS regulation, APHIS may make a determination of nonregulated status for a product following the submission of a petition requesting such a determination. The petition process can be a multi-year process that varies based on a number of factors, including APHIS's familiarity with similar products, the type and scope of the environmental review conducted, and the number and types of public comments received. APHIS conducts a comprehensive science-based review of the petition to assess, among other things, plant pest risk, environmental considerations pursuant to the National Environmental Policy Act of 1969, or NEPA, and any potential impact on endangered species. If, upon the completion of the review, APHIS grants the petition, the product is no longer deemed a "regulated article" and the petitioner may commercialize the product, subject to any conditions set forth in the decision. In January 2017, APHIS proposed significant amendments to its Part 340 regulatory framework that would, among other things, clarify the types of genetically engineered plants subject to regulation thereunder. In November 2017, however, APHIS withdrew its proposed rule and stated that it would "begin a fresh stakeholder engagement aimed at exploring alternative policy approaches." That process appears to remain ongoing.

On May 4, 2018, the USDA issued a proposed rule implementing the National Bioengineered Food Disclosure Standard, with a proposed compliance date of January 1, 2020. Under this proposed rule, the label of a bioengineered, or BE, food must include a disclosure that the food is a BE food or contains a BE ingredient, with certain exceptions. This proposed rule defines BE food as "a food that contains genetic material that was has been modified through *in vitro* recombinant deoxyribonucleic acid, or DNA, techniques and for which the modification could not otherwise be obtained through conventional breeding or found in nature," except in the case of an incidental additive present in food at an insignificant level and that does not have any technical or functional effect in the food. The USDA's proposed rule may change significantly prior to being finalized.

The FDA's oversight of food safety and security is primarily carried out by the Center for Food Safety and Applied Nutrition. To execute its responsibilities, the FDA conducts inspections and collects and analyzes product samples. Foods are typically not subject to premarket review and approval requirements, with limited exceptions, such as the requirement for premarket review and approval of food additives. Under Section 201(s) and 409 of the FDCA, any substance that is reasonably expected to become a component of food is considered a "food additive" that is subject to premarket approval by the FDA, unless it is already subject to a food additive regulation. Ingredients that are GRAS are exempt from the definition of food additive and from the premarket approval requirements. Under section 201(s), and FDA's implementing regulations, the use of a food substance may be GRAS either through a determination by qualified experts or, for a substance used in food before 1958, through experience based on common use in food.

Manufacturers of GRAS substances may voluntarily provide the FDA with a notification of GRAS determination, which includes, among other things, a description of the substance, the applicable conditions of use, the dietary exposure and an explanation of how the substance was determined to be safe for the intended use. Upon review of such a notification, the FDA may respond with a "no questions" letter stating that while it has not made its own GRAS determination, it has no questions at the time regarding the applicant's own GRAS determination. Alternatively, manufacturers may self-affirm that a given substance is GRAS without the voluntary FDA notification. A company may market a new food ingredient based on its independent determination that the substance is GRAS; however, the FDA can disagree with this determination and take enforcement action.

The FDA regulates foods made with genetically modified organisms under the approach summarized in its 1992 "Statement of Policy: Foods Derived from New Plant Varieties." Under this policy, updated in 2017, the FDA regulates foods derived from genetically modified plant varieties consistent with the framework for non-genetically modified foods. Under this framework, the FDA offers a voluntary consultation process to determine whether a food derived from a genetically modified plant variety raises any safety or other regulatory issues, such as whether any substance in the food from the plant may require premarket approval as a food additive.

Foreign Regulation

Medicinal products

Clinical trials. Clinical trials of medicinal products in the European Economic Area ("EEA") (which is comprised of the 27 Member States of the EU plus Norway, Iceland and Liechtenstein) must be conducted in accordance with European Union and national regulations and the International Conference on Harmonization ("ICH") guidelines on GCPs. Additional GCP guidelines from the European Commission, focusing in particular on traceability, apply to clinical trials of advanced therapy medicinal products. If the sponsor of the clinical trial is not established within the EEA, it must appoint an entity within the EEA to act as its legal representative. The sponsor must take out a clinical trial insurance policy, and in most countries, the sponsor is liable to provide 'no fault' compensation to any study subject injured in the clinical trial.

Prior to commencing a clinical trial, the sponsor must obtain a clinical trial authorization ("CTA"), from the competent authority, and a positive opinion from an independent ethics committee. The application for a CTA must include, among other things, a copy of the trial protocol and an investigational medicinal product dossier containing information about the manufacture and quality of the medicinal product under investigation. Currently, clinical trial authorization applications must be submitted to the competent authority in each member state in which the trial will be conducted. Under the new Regulation on Clinical Trials, which is currently expected to take effect in 2022, there will be a centralized application procedure where one national authority takes the lead in reviewing the application and the other national authorities have only a limited involvement. Any substantial changes to the trial protocol or other information submitted with the CTA applications must be notified to or approved by the relevant competent authorities and ethics committees. Investigational medicinal products used in clinical trials must be manufactured in accordance with the cGMPs specified in EudraLex, Volume 4, Annex 13 and certified by a Qualified Person before use. Other national and EEA-wide regulatory requirements may also apply.

Marketing authorizations. To market a medicinal product in the EEA, we must obtain a Marketing Authorization ("MA"). There are two types of MAs:

- The Union MA, which is issued by the European Commission through the Centralized Procedure, based on the opinion of the Committee for Medicinal Products for Human Use ("CHMP") of the European Medicines Agency ("EMA") and which is valid throughout the entire territory of the EEA. The Centralized Procedure is mandatory for certain types of products, such as medicinal products derived from biotechnology processes, orphan designated medicinal products, advanced therapy medicinal products (such as gene therapy, somatic cell therapy and tissue engineered products), and medicinal products containing a new active substance indicated for the treatment certain diseases, such as AIDS, cancer, neurodegenerative disorders, diabetes, auto immune and viral diseases. The Centralized Procedure is optional for products containing a new active substance not yet authorized in the EEA, 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 maximum timeframe for the evaluation of an MA application is 210 days, excluding clock stops. Accelerated evaluation might be granted by the CHMP in exceptional cases, when a medicinal product is of major interest from the point of view of public health and in particular from the viewpoint of therapeutic innovation. If the CHMP accepts such request, the time limit of 210 days will be reduced to 150 days but it is possible that the CHMP can revert to the standard time limit for the centralized procedure if it considers that it is no longer appropriate to conduct an accelerated assessment.
- National MAs, which are issued by the competent authorities of the Member States of the EEA 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 EEA, 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 authority 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.

Under the above described procedures, in order to grant the MA, the EMA or the competent authorities of the Member States of the EEA make an assessment of the risk benefit balance of the product on the basis of scientific criteria concerning its quality, safety and

efficacy. MAs have an initial duration of five years. After these five years, the authorization may be renewed on the basis of a reevaluation of the risk-benefit balance.

Priority medicines scheme. Innovative products that target an unmet medical need and are expected to be of major public health interest may be eligible for a number of expedited development and review programs, such as the so-called Priority Medicines ("PRIME") scheme, which provides incentives similar to the breakthrough therapy designation in the U.S. PRIME was launched in 2016 by the EMA to support the development and accelerate the review of new therapies to treat patients with unmet medical need. This voluntary scheme is based on enhanced interaction and early dialogue with developers of promising medicines, to optimize development plans and speed up evaluation so these medicines can reach patients earlier. To qualify for PRIME, product candidates require early clinical evidence that the therapy has the potential to offer a therapeutic advantage over existing treatments or benefits patients without treatment options. Among the benefits of PRIME are the appointment of a rapporteur to provide continuous support and help build knowledge ahead of an MA application, early dialogue and scientific advice at key development milestones, and the potential to qualify products for accelerated review earlier in the application process. Innovative medicines fulfilling a medical need may also benefit from different types of fast track approvals, such as a conditional marketing authorization or a marketing authorization under exceptional circumstances granted on the basis of less comprehensive clinical data than normally required (respectively in the likelihood that the sponsor will provide such data within an agreed timeframe or when comprehensive data cannot be obtained even after authorization).

Advanced therapy classification. Based on legislation adopted in 2007, the EMA established an additional regulatory designation for products classified as an advanced therapy medicinal product ("ATMP"). The ATMP designation offers sponsors a variety of benefits similar to those associated with the PRIME scheme, including scientific and regulatory guidance, additional opportunities for dialogue with regulators, and presubmission review and certification of the CMC and nonclinical data proposed for submission in a forthcoming MA applications for micro-,small-, or medium-sized enterprises. To qualify for this designation, product candidates intended for human use must be based on gene therapy, somatic cell therapy, or tissue engineered therapy.

Data and marketing exclusivity. In the EEA, new products authorized for marketing, or reference products, qualify for eight years of data exclusivity and an additional two years of market exclusivity upon marketing authorization. The data exclusivity period prevents generic or biosimilar applicants from relying on the pre-clinical and clinical trial data contained in the dossier of the reference product when applying for a generic or biosimilar marketing authorization in the EU during a period of eight years from the date on which the reference product was first authorized in the EU. The market exclusivity period prevents a successful generic or biosimilar applicant from commercializing its product in the EU until 10 years have elapsed from the initial authorization of the reference product in the EU. The 10-year market exclusivity period can be extended to a maximum of eleven years if, during the first eight years of those 10 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 held to bring a significant clinical benefit in comparison with existing therapies.

Pediatric development. In the EEA, MA applications for new medicinal products have to include the results of studies conducted in the pediatric population, in compliance with a pediatric investigation plan ("PIP"), agreed with the EMA's Pediatric Committee (" PDCO"). 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 these 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. Once the MA is obtained in all member states of the EU and study results are included in the product information, even when negative, the product is eligible for six months' supplementary protection certificate extension (if any is in effect at the time of authorization) or, in the case of orphan products, a two year extension of the orphan market exclusivity.

Orphan drug designation. In the EEA, a medicinal product can be designated as an orphan drug 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; and (2) either (a) such condition affects not more than five in ten thousand persons in the EU when the application is made, or (b) without incentives, it is unlikely that the marketing of the product in the EU would generate sufficient return to justify the necessary investment; and (3) there exists no satisfactory method of diagnosis, prevention or treatment of the condition in question that has been authorized in the EU or, if such method exists, the product will be of significant benefit to those affected by that condition.

In the EEA, an application for designation as an orphan product can be made any time prior to the filing of a MA application.

MA for an orphan drug leads to a ten-year period of market exclusivity. During this market exclusivity period, the EMA or the member state competent authorities, cannot accept another application for a MA, or grant a MA, for a similar medicinal product for the same indication. The period of market exclusivity is extended by two years for medicines that have also complied with an agreed PIP.

This period may, however, be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for orphan drug designation, for example because the product is sufficiently profitable not to justify market exclusivity. Market exclusivity can be revoked only in very selected cases, such as consent from the marketing authorization holder, inability to supply sufficient quantities of the product, demonstration of "clinical superiority" by a similar medicinal product, or, after a review by the Committee for Orphan Medicinal Products, requested by a member state in the fifth year of the marketing exclusivity period (if the designation criteria are believed to no longer apply).

Medicinal products designated as orphan drugs are eligible for incentives made available by the EU and its Member States to support research into, and the development and availability of, orphan drugs. Orphan designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

Genetically Modified Food Products

In the EEA food products are generally governed by Regulation (EC) No 178/2002 laying down the general principles and requirements of food law as well as the procedures in matters of food safety and establishing the European Food Safety Authority ("EFSA"). Food business operators are regulated by, among other authorities, the European Commission and EFSA, and national food safety authorities in EEA countries. In addition, food additives (such as substances preserving, coloring or sweetening food) are specifically regulated by Regulation (EC) No 1333/2008, which sets the conditions of use and labeling requirements for additives, and Commission Regulation (EU) No 234/2011, which establishes a common authorization procedure for food improvement agents (including food additives). To be used on the EEA market, additives must be safe and authorized by the European Commission for that purpose. EFSA and/or the Scientific Committee on Food assess the safety of food additives. Authorized additives and their conditions of use are listed in a European list. For some categories of food additives, additional requirements may apply.

A genetically modified organism ("GMO") is an organism, with the exception of human beings, in which the genetic material has been altered in a way that does not occur naturally by mating and/or natural recombination. In July 2018, the Court of Justice of the European Union ("CJEU") clarified in its ruling C-528/16 that organisms from new mutagenesis techniques also fall within the scope of the European GMO legislation. Food which contains or consists of such GMOs, or is produced from GMOs, is called genetically modified food, and is regulated by a number of specific EU and national regulations. In particular, Regulation (EC) No. 1829/2003 on genetically modified food and feed (complemented by Commission Implementing Regulation (EU) No 503/2013) and Directive 2001/18/EC on the deliberate release of GMOs into the environment (as amended by Commission Directive (EU) 2018/350) provide that both the cultivation of GMOs and the use of GMOs in food, feed and derived products in the EEA are subject to prior authorizations. Authorizations for these respective activities are granted by the national competent authorities of EEA countries following a thorough risk assessment (of the risks the GMO may present to the environment, human health and animal safety) by EFSA. Authorizations are valid throughout the EEA, for a maximum of 10 years, and are renewable. In accordance with Directive (EU) 2015/412 individual countries may further restrict or prohibit GMO cultivation on their territory. The European Commission holds and maintains a register of genetically modified food and feed which is available to the general public.

GMO operators must also comply with traceability and labeling requirements as notably provided for in Regulation (EC) No 1830/2003. All operators, such as farmers or food and feed producers, which introduce such products in the supply chain or purchase such products, must be able to identify their supplier and the companies to which the products have been delivered. Operators must provide their customers with an indication that the product – or certain ingredients – contains, consists of, or is obtained from GMOs, and information on the unique identifier(s) for these GMOs. Operators must keep a record for a five year period after every transaction. In addition, subject to an exception of a proportion no higher than 0.9 percent of the food/feed ingredients considered individually, the list of ingredients on the labeling of pre-packed genetically modified food/feed products must indicate "genetically modified" or "produced from genetically modified [name of the organism]." For products without packaging, this information must be clearly displayed in close proximity to the product.

Specific post-authorization requirements apply. For instance, GMO operators must implement and regularly report on a post-market environmental monitoring plan, including general surveillance for unanticipated adverse effects and case-specific monitoring to detect direct and indirect effects which have been identified in the environmental risk assessment. In addition, post-market monitoring plans may be requested in specific cases to ensure that the conditions of use are duly applied and to monitor the consumption of the product. Further to Regulation (EU) 2017/625, GMOs are subject to official controls by EEA countries for the deliberate release of GMOs in the EEA and the presence of GMOs and/or genetically modified material in food, feed and seeds at import stage and on the EEA market. Official controls, which may consist of audits and inspections, verify the absence of unauthorized GMOs and genetically modified material on the EEA market and check proper traceability and labeling.

Transboundary movements of GMOs are regulated by Regulation (EC) 1946/2003 which transposes the Cartagena Protocol on Biosafety into EU law. The Regulation obliges countries to take legal, administrative and other measures to implement their commitments under the Protocol, and in particular addresses GMOs exports, requiring a notification to importing parties, information to the Biosafety Clearing House as well as other identification and accompanying documentation.

Even though EU regulations are directly applicable in all EU Member States and – when specified – in Iceland, Liechtenstein and Norway, additional national laws, regulations, implementing rules and guidelines on specific aspects may impose further requirements on GMOs operators.

GMOs and modern biotechnologies are under scrutiny in the EEA. As a variety of new techniques, based on advances in biotechnology, has been developed in the last decade, the European Commission follows these developments to strike a balance between innovation in the food and agricultural sector while maintaining high safety standards. In November 2019, the Council of the European Union requested the European Commission to provide a study on new genomic techniques, the results of which are expected by April 30, 2021.

Other U.S. Healthcare Laws and Compliance Requirements

In the United States, our activities are potentially subject to regulation under various federal and state healthcare laws including, among others, the federal Anti-Kickback Statute, the federal False Claims Act and HIPAA. Similar laws exist in foreign jurisdictions including the EEA, as well.

The U.S. federal Anti-Kickback Statute prohibits, among other things, any person or entity, from knowingly and willfully offering, paying, soliciting or receiving any remuneration, directly or indirectly, overtly or covertly, in cash or in kind, to induce or in return for purchasing, leasing, ordering or arranging for the purchase, lease or order of any item or service reimbursable under Medicare, Medicaid or other federal healthcare programs. The term remuneration has been interpreted broadly to include anything of value. A person does not need to have knowledge of the statute or specific intent to violate it to have committed a violation.

The U.S. federal civil and criminal false claims laws, including the civil False Claims Act, which can be enforced through civil whistleblower or qui tam actions, and civil monetary penalties laws, prohibit, among other things, any person or entity from knowingly presenting, or causing to be presented, a false claim for payment to, or approval by, the federal government or knowingly making, using, or causing to be made or used a false record or statement material to a false or fraudulent claim to the federal government, or from knowingly making a false statement to avoid, decrease or conceal an obligation to pay money to the U.S. government. In addition, the government may assert that a claim including items or services resulting from a violation of the U.S. federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act.

The U.S. Health Insurance Portability and Accountability Act of 1996, or HIPAA, created additional federal criminal statutes that prohibit 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 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. Similar to the U.S. 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.

Additionally, the federal Physician Payments Sunshine Act, 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) to report annually to CMS information related to certain payments or other transfers of value made or distributed to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain other health care professionals beginning in 2022, and teaching hospitals, or to entities or individuals at the request of, or designated on behalf of, the physicians and teaching hospitals and to report annually to CMS certain ownership and investment interests held by physicians and their immediate family members.

Moreover, analogous state and non-U.S. laws and regulations may apply to our activities, such as state anti-kickback and false claims laws, which may apply to our business practices, including, but not limited to, research, distribution, sales and marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers, or by the patients themselves, state laws that require pharmaceutical and device companies to comply with the industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the U.S. government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources, state and local laws and regulations that require manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures and pricing information, and state and local laws which require the registration of pharmaceutical sales representatives.

Efforts to ensure that current and future business arrangements with third parties comply with applicable healthcare laws and regulations involves substantial costs. If a business is found to be in violation of any of these or any other health regulatory laws that may apply to it, it may be subject to significant penalties, including the imposition of significant civil, criminal and administrative

penalties, damages, monetary fines, disgorgement, individual imprisonment, possible exclusion from participation in Medicare, Medicaid and other U.S. healthcare programs, additional reporting requirements and oversight if subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, contractual damages, reputational harm, diminished profits and future earnings, and curtailment or restructuring of operations.

Coverage, Pricing and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status for newly approved therapeutics. In the United States and markets in other countries, sales of any products for which we receive regulatory approval for commercial sale will depend, in part, on the extent to which third-party payors provide coverage, and establish adequate reimbursement levels for such products. In the United States, third-party payors include federal and state healthcare programs, private managed care providers, health insurers and other organizations. For products administered under the supervision of a physician, obtaining coverage and adequate reimbursement may be particularly difficult because of the higher prices often associated with such drugs. A payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a product does not assure that other payors will also provide coverage for the product. Moreover, the coverage provided may be more limited than the purposes for which the product is approved by the FDA. It is also possible that a third-party payor may consider a product as substitutable and only offer to reimburse patients for the less expensive product. Adequate third-party payor reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development. Coverage policies and third-party payor reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

In the EEA, governments influence the price of products through their pricing and reimbursement rules and control of national health care systems that fund a large part of the cost of those products to consumers. Member States are free to restrict the range of pharmaceutical products for which their national health insurance systems provide reimbursement, and to control the prices and reimbursement levels of pharmaceutical products for human use. Some jurisdictions operate positive and negative list systems under which products may only be marketed once a reimbursement price has been agreed to by the government. Member states may approve a specific price or level of reimbursement for the pharmaceutical product, or alternatively adopt a system of direct or indirect controls on the profitability of the company responsible for placing the pharmaceutical product on the market, including volume-based arrangements, caps and reference pricing mechanisms. To obtain reimbursement or pricing approval, some of these countries may require the completion of clinical trials that compare the cost effectiveness of a particular product candidate to currently available therapies. Other member states allow companies to fix their own prices for medicines, but monitor and control company profits. The downward pressure on health care costs in general, particularly prescription products, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, in some countries, cross border imports from low-priced markets exert a commercial pressure on pricing within a country.

Healthcare Reform

In the United States and some foreign jurisdictions, there have been, and continue to be, several legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of product candidates, restrict or regulate post-approval activities, and affect the ability to profitably sell product candidates for which marketing approval is obtained. Among policy makers and payors in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access. The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, collectively the Affordable Care Act, enacted in March 2010, has substantially changed healthcare financing and delivery by both governmental and private insurers. Among other things the Affordable Care Act included the following provisions:

- an annual, nondeductible fee on any entity that manufactures or imports certain specified branded prescription drugs and biologic agents apportioned among these entities according to their market share in some government healthcare programs;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program;
- a new Medicare Part D coverage gap discount program, in which manufacturers must now agree to point-of-sale discounts of 70% off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturers' outpatient drugs to be covered under Medicare Part D;
- extension of manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;
- expansion of eligibility criteria for Medicaid programs;
- expansion of the entities eligible for discounts under the 340B Drug Discount Program;

- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;
- 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; and
- a licensure framework for follow on biologic products.

On December 14, 2018, a U.S. District Court Judge in the Northern District of Texas, or Texas District Court Judge, ruled that the entire Affordable Care Act is invalid based primarily on the fact that the legislation enacted on December 22, 2017, the Tax Cuts and Jobs Act of 2017, or the TCJA, repealed the tax-based shared responsibility payment imposed by the Affordable Care Act, on certain individuals who fail to maintain qualifying health coverage for all or part of a year, which is commonly referred to as the "individual mandate." On December 18, 2019, the U.S. Court of Appeals for the 5th Circuit upheld the district court's decision that the individual mandate was unconstitutional but remanded the case back to the District Court to determine whether the remaining provisions of the ACA are invalid as well. The U.S. Supreme Court is currently reviewing the case, although it remains unclear when or how the Supreme Court will rule. It is also unclear how other efforts, if any, to challenge, repeal or replace the Affordable Care Act will impact the Affordable Care Act.

In addition, other legislative changes have been proposed and adopted since the Affordable Care Act was enacted. On August 2, 2011, the Budget Control Act of 2011 was signed into law, which, among other things, included reductions to Medicare payments to providers of 2% per fiscal year, which went into effect on April 1, 2013 and, due to subsequent legislative amendments to the statute will remain in effect through 2030, with the exception of a temporary suspension from May 1, 2020 through March 31, 2021, unless additional Congressional action is taken. On January 2, 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, reduced Medicare payments to several providers, including hospitals, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

Additionally, 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 are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a drug manufacturer to make its drug products available to eligible patients as a result of the Right to Try Act.

Finally, there has been heightened governmental scrutiny recently over pharmaceutical pricing practices in light of the rising cost of prescription drugs and biologics. Such scrutiny has resulted in several recent Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies, rebates and price negotiation for pharmaceutical products. How the incoming Biden Administration chooses to prioritize such reforms and other policy initiatives, and how such events may impact our ability to realize returns on our product development investments remains to be seen. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical product and medical device pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and medical devices to purchase and which suppliers will be included in their prescription drug and other healthcare programs.

Data Privacy and Security

Numerous state, federal and foreign laws, including consumer protection laws and regulations, govern the collection, dissemination, use, access to, confidentiality and security of personal information, including health-related information. In the United States, numerous federal and state laws and regulations, including data breach notification laws, health information privacy and security laws, including HIPAA, and federal and state consumer protection laws and regulations (e.g., Section 5 of the FTC 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 partners. In addition, certain state and non-U.S. laws, such as the California Consumer Privacy Act, or the CCPA, the California Privacy Rights Act, or the CPRA, and the EU General Data Protection Regulation, or the GDPR, govern the privacy and security of personal information, including health-related information in certain circumstances, some of which are more stringent than HIPAA and 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/or criminal penalties and private litigation. Privacy and security laws, regulations, and other obligations are constantly evolving, may conflict with each other to complicate compliance efforts, and can result in investigations, proceedings, or actions that lead to significant civil and/or criminal penalties and restrictions on data processing.

Human Capital

We are a purpose-driven organization, and we have carefully promoted a culture that values innovation, accountability, respect, adaptability and perseverance. We strive to ensure that our open, collaborative culture empowers Precisioneers to be their best selves and do their best work. We strongly believe that our shared values will help our team navigate and overcome challenges we may experience as we pursue our mission of improving life through genome editing. Our culture has helped build a world-class team with industry-leading experience in genome editing and we believe this will continue to attract new talent to further build our capabilities. Our team is a group of motivated individuals that value the opportunity to contribute their time and talents toward the pursuit of improving life. We believe all Precisioneers appreciate high-quality research and are moved by the opportunity to translate their work into treatments and solutions that could impact human health.

We are a company and a community dedicated to improving life. This isn't just a statement supporting the products that we are developing – it is a statement that speaks to our collective desire to do our part in improving the lives of those around us. Through our newly launched Diversity and Inclusion initiative, we are actively fostering an environment that attracts the best talent, values diversity of life experiences and perspectives, and encourages innovation in pursuit of our mission. With guest lectures, new trainings, employee resource groups, and other activities, we are supporting a workplace that reflects and embraces the gender, race, ethnicity, sexual orientation, age, physical ability, as well as all cultural backgrounds in our community.

Notable benefits we offer to our full-time Precisioneers include:

- employer sponsored health insurance;
- employer 401(k) matching contributions;
- generous paid time off policies;
- wellness programs including employee assistance programs, wellness reimbursement, and an on-site gym; and
- professional development programs including a tuition reimbursement program

The health and safety of our Precisioneers is also a top priority. The global effects associated with the COVID-19 pandemic have been unprecedented in their scope and depth. We have implemented measures to mitigate exposure risks and support operations. We initiated a health and safety program addressing mandatory use of face masks, social distancing, sanitary handwashing practices, use of personal protective equipment stations, stringent cleaning and sanitization of all facilities and measures to reduce total occupancy in facilities. We have implemented temperature and symptom screening procedures at each location, and we have continuously communicated to all our Precisioneers that if they are not comfortable coming to work, regardless of role, then they do not have to do so. Throughout this crisis, our focus has been on keeping our workplace as safe as possible, while ensuring business continuity and positioning ourselves well for the future.

As of December 31, 2020, we had 231 full-time Precisioneers, comprised of 208 from our Therapeutics Segment and 23 from our Food Segment. Of these full-time employees, 184 are engaged in research and development activities and 57 have Ph.D. degrees. None of our employees are represented by a labor union or covered by a collective bargaining agreement.

Corporate Information

We were incorporated in Delaware in January 2006. Our principal executive offices are located at 302 East Pettigrew St., Suite A-100, Durham, North Carolina 27701, and our telephone number is (919) 314-5512. Our website address is www.precisionbiosciences.com. The information contained in, or accessible through, our website does not constitute a part of this Annual Report on Form 10-K.

Available Information

We file annual, quarterly and current reports, proxy statements and other information with the U.S. Securities and Exchange Commission ("SEC"). Our SEC filings are available to the public over the Internet at the SEC's website at *www.sec.gov*. Our SEC filings are also available free of charge under the Investors and Media section of our website at *www.precisionbiosciences.com* as soon as reasonably practicable after they are filed with or furnished to the SEC. Our website and the information contained on or connected to that site are not incorporated into this Annual Report on Form 10-K.

We may use our website as a distribution channel of material information about the Company. Financial and other important information regarding the Company is routinely posted on and accessible through the Investors and Media section of our website at *www.precisionbiosciences.com*. In addition, you may automatically receive email alerts and other information about the Company when you enroll your email address by visiting the "Email Alerts" option under Investor Tools of the Investors and Media section of our website at *www.precisionbiosciences.com*.

Item 1A. Risk Factors.

Investing in our common stock involves a high degree of risk. Before investing in our common stock, you should consider carefully the risks described below, together with the other information included or incorporated by reference in this Annual Report on Form 10-K. The occurrence of any of the following risks could materially adversely affect our business, financial condition, results of operations and future growth prospects. In these circumstances, the market price of our common stock could decline, and you may lose all or part of your investment.

Risks Related to Our Financial Condition, Limited Operating History and Need for Additional Capital

We have incurred significant operating losses since our inception and expect to continue to incur losses for the foreseeable future. We have never been profitable, and may never achieve or maintain profitability.

We have never been profitable and do not expect to be profitable in the foreseeable future. Since inception, we have incurred significant operating losses. If our product candidates are not successfully developed and approved, we may never generate any revenue from product sales. Our net losses were $109.0 million for the year ended December 31, 2020 and $92.9 million for the year ended December 31, 2019. As of December 31, 2020, we had an accumulated deficit of $286.1 million. In addition, we have not commercialized any products and have never generated any revenue from product sales. Substantially all of our losses have resulted from expenses incurred in connection with our research and development activities, including our preclinical development activities, and from general and administrative costs associated with our operations. We have financed our operations primarily through our IPO, private placements of our convertible preferred stock and convertible debt and payments under development, collaboration and license agreements. The amount of our future net losses will depend, in part, on the amount and growth rate of our expenses and our ability to generate revenues.

All of our current or future product candidates will require substantial additional development time and resources before we may realize revenue from product sales, if at all. We expect to continue to incur significant expenses and operating losses for the foreseeable future. Our expenses have increased and we anticipate will continue to increase substantially if and as we:

- continue our current research and development programs, including conducting laboratory, preclinical and greenhouse studies for product candidates;
- continue to conduct or initiate clinical or field trials for product candidates;
- seek to identify, assess, acquire or develop additional research programs or product candidates;
- maintain, expand and protect our intellectual property portfolio;
- seek marketing approvals for any product candidates that may successfully complete development;
- establish a sales, marketing and distribution infrastructure to commercialize any products that may obtain marketing approval;
- further develop and refine the manufacturing process for our product candidates;
- change or add additional manufacturers or suppliers of biological materials or product candidates;
- further develop our genome editing technology;
- acquire or in-license other technologies;
- seek to attract and retain new and existing personnel;
- expand our facilities; and
- incur increased costs as a result of operating as a public company.

It will be several years, if ever, before we obtain regulatory approval for, and are ready for commercialization of, a therapeutic product candidate. Similarly, no product candidate from our food platform has advanced to field testing, and it will be several years, if ever, before we or our collaborators commercialize any such product candidate. New food and agriculture products using the precise editing approach generally take approximately three to five years to develop. Even if a therapeutic product candidate receives regulatory approval or a food or agriculture product advances through commercialization, future revenues for such product candidate will depend upon many factors, such as, as applicable, the size of any markets in which such product candidate is approved for sale, the market share captured by such product candidate, including as a result of the market acceptance of such product candidate and the effectiveness of manufacturing, sales, marketing and distribution operations related to such product candidate, the terms of any collaboration or other strategic arrangement we may have with respect to such product candidate and levels of reimbursement from

third-party payors. If we are unable to develop and commercialize one or more product candidates either alone or with collaborators, or if revenues from any product candidate that receives marketing approval or is commercialized are insufficient, we may not achieve profitability. Even if we do achieve profitability, we may not be able to sustain or increase profitability. If we are unable to achieve and maintain profitability, the value of our common stock will be materially adversely affected.

We will need substantial additional funding, and if we are unable to raise a sufficient amount of capital when needed on acceptable terms, or at all, we may be forced to delay, reduce or eliminate some or all of our research programs, product development activities and commercialization efforts.

The process of identifying product candidates and conducting preclinical or greenhouse studies and clinical or field trials is time consuming, expensive, uncertain and takes years to complete. We expect our expenses to increase in connection with our ongoing activities, particularly as we identify, continue the research and development of, initiate and continue clinical or field trials of, and seek marketing approval for, product candidates. In addition, if any therapeutic product candidate that we develop alone or with collaborators obtains marketing approval, we may incur significant commercialization expenses related to product manufacturing, sales, marketing and distribution efforts. Furthermore, we have incurred, and expect to continue to incur additional costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise sufficient capital when needed, we may be forced to delay, reduce or eliminate current or future research programs, product development activities and/or commercialization efforts.

We believe that our cash and cash equivalents as of December 31, 2020, cash payments received from Lilly in January 2021 in connection with the closing of the Development and License Agreement, expected operational receipts and available credit will allow the Company to continue its operations into 2023. We have based this estimate on assumptions that may prove to be wrong, and we could use our capital resources sooner than we currently expect. Our operating plans and other demands on our cash resources may change as a result of many factors, including factors unknown to us, 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. We do not currently expect future grant revenues to be a material source of revenue.

Attempting to secure additional financing may divert our management from our day-to-day activities, which may adversely affect our ability to develop product candidates. Our future capital requirements will depend on many factors, including:

- the timing, scope, progress, costs, results and analysis of results of research activities, preclinical or greenhouse studies and clinical or field trials for any of our product candidates;
- the costs of future activities, including product manufacturing, sales, marketing and distribution activities for any product candidates that receive regulatory approval;
- the success of our existing collaborative relationships;
- the extent to which we exercise any development or commercialization rights under collaborative relationships;
- our ability to establish and maintain additional collaborative relationships on favorable terms, or at all;
- the extent to which we expand our operations and the timing of such expansion, including with respect to facilities, employees and product development platforms;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property and proprietary rights and defending intellectual property-related claims;
- the extent to which we acquire or in-license other technologies or product candidates;
- the extent to which we acquire or invest in other businesses;
- the costs of continuing to operate as a public company; and
- the amount of revenues, if any, received from commercial sales of any products that we develop alone or with collaborators that receive regulatory approval.

Even if we believe we have sufficient funds for our current or future operating plans, we may continue to seek additional capital if market conditions are favorable or in light of specific strategic considerations. Adequate additional financing may not be available to us on acceptable terms, or at all. If we are unable to obtain sufficient funding on a timely basis or on favorable terms, we may be required to significantly delay, reduce or eliminate one or more of our research or product development programs and/or commercialization efforts. We may also be unable to expand our operations or otherwise capitalize on business opportunities as desired. Any of these events could materially adversely affect our financial condition and business prospects.

Provisions of our debt instruments may restrict our ability to pursue our business strategies.

Pursuant to the Pacific Western Loan Agreement (as defined below) with Pacific Western Bank ("PWB"), we may request advances on a revolving line of credit ("the Revolving Line") of up to an aggregate principal of $30.0 million, the maturity date of the Revolving Line is June 23, 2023. As of December 31, 2020, we had no borrowings under our Revolving Line. Under the loan and security agreement, we granted PWB a security interest in substantially all of our assets, excluding any of the intellectual property now or hereafter owned, acquired or received by us (but including any rights to payment from the sale or licensing of any such intellectual property).

The Pacific Western Loan Agreement requires us, and any debt instruments we may enter into in the future may require us, to comply with various covenants that limit our ability to, among other things:

- dispose of assets;
- change our name, location, executive office or executive management, business, fiscal year, or control;
- complete mergers or acquisitions;
- incur indebtedness;
- encumber assets;
- pay dividends or make other distributions to holders of our capital stock;
- make specified investments;
- make capitalized expenditures in excess of $40 million in the aggregate during each fiscal year;
- maintain less than $10.0 million of unrestricted cash at PWB; and
- engage in certain transactions with our affiliates.

These restrictions could inhibit our ability to pursue our business strategies. In addition, we are subject to financial covenants based on minimum cash balances.

Raising additional capital may cause dilution to our stockholders restrict our operations or require us to relinquish rights to our technologies or product candidates.

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity and/or debt financings and collaborations, licensing agreements or other strategic arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms of such securities may include liquidation or other preferences that adversely affect your rights as a common stockholder. To the extent that we raise additional capital through debt financing, it would result in increased fixed payment obligations and a portion of our operating cash flows, if any, being dedicated to the payment of principal and interest on such indebtedness. In addition, debt financing may involve agreements that include restrictive covenants that impose operating restrictions, such as restrictions on the incurrence of additional debt, the making of certain capital expenditures or the declaration of dividends. To the extent we raise additional capital through arrangements with collaborators or otherwise, we may be required to relinquish some of our technologies, research programs, product development activities, product candidates and/or future revenue streams, license our technologies and/or product candidates on unfavorable terms or otherwise agree to terms unfavorable to us. Furthermore, any capital raising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to advance research programs, product development activities or product candidates.

We have a limited operating history, which makes it difficult to evaluate our current business and future prospects and may increase the risk of your investment.

We are a genome editing company with a limited operating history. We formed our company in 2006 and spent the first nine years of our company's history developing and refining our core technology, and only during the past several years have we focused our efforts on advancing the development of product candidates.

Investment in biopharmaceutical and agricultural biotechnology product development is a highly speculative endeavor. It entails substantial upfront capital expenditures, and there is significant risk that any product candidate will fail to demonstrate adequate efficacy or an acceptable safety profile, obtain any required regulatory approvals or become commercially viable. Our genome editing platform and the technologies we are using are new and unproven. We have initiated a Phase 1/2a clinical trial in patients with R/R NHL and R/R B-ALL, a Phase 1/2a clinical trial in patients with NHL, chronic lymphocytic leukemia, or CLL, and small lymphocytic

lymphoma, or SLL, as well as a Phase 1/2a clinical trial in patients with R/R multiple myeloma, but we have not commenced field trials for any of our product candidates from our food platform. We have not yet demonstrated an ability to successfully complete any clinical or field trials, obtain any required marketing approvals, manufacture products, conduct sales, marketing and distribution activities, or arrange for a third party to do any of the foregoing on our behalf. Consequently, any predictions made about our future success or viability may not be as accurate as they could be if we had a history of successfully developing and commercializing products.

Additionally, we encounter risks and difficulties frequently experienced by new and growing companies in rapidly developing and changing industries, including challenges in forecasting accuracy, determining appropriate investments of our limited resources, gaining market acceptance of our technology, managing a complex regulatory landscape and developing new product candidates, which may make it more difficult to evaluate our likelihood of success. Our current operating model may require changes in order for us to adjust to these challenges or scale our operations efficiently. Our limited operating history, particularly in light of the rapidly evolving nature of the biopharmaceutical and agricultural biotechnology industries and the genome editing field, may make it difficult to evaluate our technology and business prospects or to predict our future performance. Additionally, due to the stage of our operations, we expect that our financial condition and operating results may fluctuate significantly from quarter to quarter as a result of many factors as we build our business, and you should not rely upon the results of any particular quarterly or annual period as indications of future operating performance.

We may expend our limited resources on pursuing particular research programs or product candidates that may be less successful or profitable than other programs or product candidates.

Research programs to identify new product candidates and product development platforms require substantial technical, financial and human resources. We may focus our efforts and resources on potential programs, product candidates or product development platforms that ultimately prove to be unsuccessful. Any time, effort and financial resources we expend on identifying and researching new product candidates and product development platforms may divert our attention from, and adversely affect our ability to continue, development and commercialization of existing research programs, product candidates and product development platforms. Clinical trials or field trials, as applicable, of any of our product candidates may never commence despite the expenditure of significant resources in pursuit of their development, and our spending on current and future research and development programs, product candidates and product development platforms may not yield any commercially viable products. As a result of having limited financial and managerial resources, we may forego or delay pursuit of opportunities that later prove to have greater commercial potential. For example, we continue to strategically assess our options in connection with a potential separation of our food segment, Elo, from Precision, which could be as early as during 2021. Our resource allocation decisions may cause us to fail to timely capitalize on viable commercial products or profitable market opportunities. Additionally, if we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other strategic arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate.

We expect to take advantage of a Research and Development Tax Incentive program in Australia, which could be amended or changed.

We may be eligible to receive a financial incentive from the Australian government as part of its Research and Development Tax Incentive program, or R&D Tax Incentive program. The R&D Tax Incentive program is one of the key elements of the Australian government's support for Australia's innovation system and, if eligible, provides the recipient with a 43.5% refundable tax offset for research and development activities in Australia. There have been recent proposals to change the structure of the innovation and research and development funding landscape in Australia, which may impact the research and development tax incentive receivable for the 2020 financial year and beyond. There can be no assurance that we will qualify and be eligible for such incentives or that the Australian government will continue to provide incentives, offset, grants and rebates on similar terms or at all.

Risks Related to the Identification, Development and Commercialization of Our Product Candidates

ARCUS is a novel technology, making it difficult to predict the time, cost and potential success of product candidate development. We have not yet been able to assess the safety and efficacy of most of our product candidates in humans, and have only limited safety and efficacy information in humans to date regarding one of our product candidates.

Our success depends on our ability to develop and commercialize product candidates using our novel genome editing technology. The novel nature of our technology makes it difficult to accurately predict the developmental challenges we may face for product candidates as they proceed through research, preclinical or greenhouse studies and clinical or field trials. There have been a limited number of clinical trials of products created with genome editing technologies, three of which have utilized our technology. Because our therapeutic research programs are all in preclinical or early clinical stages, we have only been able to assess limited safety and efficacy data for one of our product candidates in a human trial. Current or future product candidates may not meet safety and efficacy

requirements for continued development or ultimate approval in humans and may cause significant adverse events or toxicities. All of our product candidates are designed to act at the level of DNA, and because animal DNA differs from human DNA, it will be difficult for us to test our therapeutic product candidates in animal models for either safety or efficacy, and any testing that we conduct may not translate to their effects in humans. Moreover, animal models may not exist for some of the targets, diseases or indications that we intend to pursue. Similarly, we and our collaborators have not yet completed field trials for any agricultural product candidates created with our technology. Our product candidates may not be able to properly implement desired genetic edits with sufficient accuracy to be viable therapeutic or agricultural products, and there may be long-term effects associated with them that we cannot predict at this time. Any problems we experience related to the development of our genome editing technology or any of our or our collaborators' research programs or product candidates may cause significant delays or unanticipated costs, and we may not be able to satisfactorily solve such problems. These factors may prevent us or our collaborators from completing our preclinical or greenhouse studies or any clinical or field trials that we or our collaborators have ongoing or may initiate, or profitably commercializing any product candidates on a timely basis, or at all. We may also experience delays in developing a sustainable, reproducible and scalable manufacturing process as we develop and prepare to commercialize product candidates. These factors make it more difficult for us to predict the time, cost and potential success of product candidate development. If our product development activities take longer or cost more than anticipated, or if they ultimately are not successful, it would materially adversely affect our business and results of operations.

The genome editing field is relatively new and evolving rapidly, and other existing or future technologies may provide significant advantages over our ARCUS platform, which could materially harm our business.

To date, we have focused our efforts on optimizing our proprietary genome editing technology and exploring its potential applications. ARCUS is a novel genome editing technology using sequence-specific DNA-cutting enzymes, or nucleases, that is designed to perform modifications in the DNA of living cells and organisms. Other companies have previously undertaken research and development of genome editing technologies using zinc finger nucleases, transcription activator-like effector nucleases, or TALENs, and clustered regularly interspaced short palindromic repeats associated protein-9 nuclease, or CRISPR/Cas9, although none has obtained marketing approval for a product candidate developed using such technologies. Other genome editing technologies in development or commercially available, or other existing or future technologies, may lead to treatments or products that may be considered better suited for use in human therapeutics or agriculture, which could reduce or eliminate our commercial opportunity.

We are heavily dependent on the successful development and translation of ARCUS, and due to the early stages of our product development operations, we cannot give any assurance that any product candidates will be successfully developed and commercialized.

We are at an early stage of development of the product candidates currently in our programs and are continuing to develop our ARCUS technology. To date, we have invested substantially all of our efforts and financial resources to develop ARCUS and advance our current product development programs, including conducting preclinical studies, early stage clinical trials and other early research and development activities, and providing general and administrative support for these operations. We are also currently using our ARCUS technology to develop our lead in vivo gene correction programs targeting DMD and PH1. Our future success is dependent on our ability to successfully develop and, where applicable, obtain regulatory approval for, including marketing approval for, and then successfully commercialize, product candidates, either alone or with collaborators. We have not yet developed and commercialized any product candidates, and we may not be able to do so, alone or with collaborators.

Our research and development programs may not lead to the successful identification, development or commercialization of any products.

The success of our business depends primarily upon our ability to identify, develop and commercialize products using our genome editing technology. With the exception of our CD19, CD20 and BCMA product candidates, all current product candidates and product development programs are still in the discovery, preclinical or greenhouse stages. We may be unsuccessful in advancing those product candidates into clinical development or field trials or in identifying any developing additional product candidates. Our ability to identify and develop product candidates is subject to the numerous risks associated with preclinical and early stage biotechnology development activities, including that:

- the use of ARCUS may be ineffective in identifying additional product candidates;
- we may not be able to assemble sufficient resources to acquire or discover additional product candidates;
- we may not be able to enter into collaborative arrangements to facilitate development of product candidates;
- competitors may develop alternatives that render our product candidates obsolete or less attractive;
- our product candidates may be covered by third parties' patents or other exclusive rights;

- the regulatory pathway for a product candidate may be too complex, expensive or otherwise difficult to navigate successfully; or
- our product candidates may be shown to not be effective, have harmful side effects or otherwise pose risks not outweighed by such product candidate's benefits or have other characteristics that may make the products impractical to manufacture, unlikely to receive any required marketing approval, unlikely to generate sufficient market demand or otherwise not achieve profitable commercialization.

Our product candidates currently being investigated in clinical trials, or that are expected to be investigated in clinical trials, and other product candidates we may identify may never be approved. Failure to successfully identify and develop new product candidates and obtain regulatory approvals for our products would have a material adverse effect on our business and financial condition and could cause us to cease operations.

If our product candidates do not achieve projected development milestones or commercialization in the announced or expected timeframes, the further development or commercialization of such product candidates may be delayed, and our business will be harmed.

We sometimes estimate, or may in the future estimate, the timing of the accomplishment of various scientific, clinical, manufacturing, regulatory and other product development objectives. These milestones may include our expectations regarding the commencement or completion of scientific studies or clinical or field trials, the submission of regulatory filings, the receipt of marketing approval or the realization of other commercialization objectives. The achievement of many of these milestones may be outside of our control. All of these milestones are based on a variety of assumptions, including assumptions regarding capital resources, constraints and priorities, progress of and results from development activities, the receipt of key regulatory approvals or actions, and other factors, including without limitation, impacts resulting from the COVID-19 pandemic, any of which may cause the timing of achievement of the milestones to vary considerably from our estimates. If we or our collaborators fail to achieve announced milestones in the expected timeframes, the commercialization of the product candidates may be delayed, our credibility may be undermined, our business and results of operations may be harmed, and the trading price of our common stock may decline.

Adverse public perception of genome editing may negatively impact the developmental progress or commercial success of products that we develop alone or with collaborators.

The developmental and commercial success of our current product candidates, or any that we develop alone or with collaborators in the future, will depend in part on public acceptance of the use of genome editing technology for the prevention or treatment of human diseases or for application in food or agricultural products. Adverse public perception of applying genome editing technology for these purposes may negatively impact our ability to raise capital or enter into strategic agreements for the development of product candidates.

The commercial success of any food or agricultural products that we develop alone or with collaborators may be adversely affected by claims that biotechnology plant products are unsafe for consumption or use, pose risks of damage to the environment or create legal, social or ethical dilemmas. Additionally, the public may perceive any potential food or agricultural products created with ARCUS to constitute genetically modified organisms, or GMO, even if they do not constitute genetically modified organisms under relevant regulatory requirements, and may be unwilling to consume them because of negative opinions regarding consumption of genetically modified organisms. This may result in expenses, delays or other impediments to development programs in our food platform or the market acceptance and commercialization of any potential food or agricultural products.

Any therapeutic product candidates may involve editing the human genome. The commercial success of any such potential therapeutic products, if successfully developed and approved, may be adversely affected by claims that genome editing is unsafe, unethical or immoral. This may lead to unfavorable public perception and the inability of any therapeutic product candidates to gain the acceptance of the public or the medical community. Unfavorable public perceptions may also adversely impact our or our collaborators' ability to enroll clinical trials for therapeutic product candidates. Moreover, success in commercializing any therapeutic product candidates that receive regulatory approval will depend upon physicians prescribing, and their patients being willing to receive, treatments that involve the use of such product candidates in lieu of, or in addition to, existing treatments with which they are already familiar and for which greater clinical data may be available. Publicity of any adverse events in, or unfavorable results of, preclinical studies or clinical trials for any current or future product candidates, including, without limitation, patient deaths, or with respect to the studies or trials of our competitors or of academic researchers utilizing genome editing technologies, even if not ultimately attributable to our technology or product candidates, could negatively influence public opinion. Negative public perception about the use of genome editing technology in human therapeutics and food or agricultural products, whether related to our technology or a competitor's technology, could result in increased governmental regulation, delays in the development and commercialization of product candidates or decreased demand for the resulting products, any of which may have a negative impact on our business and financial condition.

We face significant competition in industries experiencing rapid technological change, and there is a possibility that our competitors may achieve regulatory approval before us or develop product candidates or treatments that are safer or more effective than ours, which may harm our financial condition and our ability to successfully market or commercialize any of our product candidates.

The development and commercialization of new drug products is highly competitive, and the genome editing field is characterized by rapidly changing technologies, significant competition and a strong emphasis on intellectual property. We will face competition with respect to our current and future therapeutic product candidates 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 of products. Competition for improving plant genetics comes from conventional and advanced plant breeding techniques, as well as from the development of advanced biotechnology traits. Other potentially competitive sources of improvement in crop yields include improvements in crop protection chemicals, fertilizer formulations, farm mechanization, other biotechnology and information management. Programs to improve genetics and crop protection chemicals are generally concentrated within a relatively small number of large companies, while non-genetic approaches are underway with a broader set of companies.

There are a number of large pharmaceutical and biotechnology companies that currently market and sell products or are pursuing the development of products for the treatment of the disease indications for which we have research programs. Some of these competitive products and therapies are based on scientific approaches that are similar to our approach, and others are based on entirely different approaches. We principally compete with others developing and utilizing genome editing technology in the human health and plant sciences sectors, including companies such as Allogene Therapeutics, Inc., Alnylam Pharmaceuticals, Inc., Caribou Biosciences, Inc., Cellectis S.A., CRISPR Therapeutics, AG, Dicerna Pharmaceuticals, Inc., Editas Medicine, Inc., Intellia Therapeutics, Inc., Sangamo Therapeutics, Inc., and Beam Therapeutics, Inc. Several companies, including Novartis Pharmaceuticals Corp. and Gilead Sciences, Inc., or Gilead, have obtained FDA approval for autologous immunotherapies, and a number of companies, including Cellectis S.A., Celgene Corp., Allogene Therapeutics and CRISPR Therapeutics AG, are pursuing allogeneic immunotherapies. We expect that our operations focused on developing products for *in vivo* gene correction will face substantial competition from others focusing on gene therapy treatments, especially those that may focus on conditions that our product candidates target. Moreover, any human therapeutics products that we develop alone or with collaborators will compete with existing standards of care for the diseases and conditions that our product candidates target and other types of treatments, such as small molecule, antibody or protein therapies. Our competitors in the agricultural biotechnology space include Pairwise Plants, LLC, Corteva Agriscience, Tropic Biosciences UK LTD, Calyxt, Inc., Benson Hill Biosystems and Cibus.

Many of our current or potential competitors, either alone or with their collaborators, have significantly greater financial resources and expertise in research and development, manufacturing, preclinical or greenhouse testing, conducting clinical or field trials, obtaining regulatory approvals and marketing approved products than we do. Mergers and acquisitions in the pharmaceutical, biotechnology and agricultural 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 we develop alone or with collaborators or that would render any such products obsolete or non-competitive. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we or our collaborators may obtain approval for any that we develop, which could result in our competitors establishing a strong market position before we are able to enter the market. Additionally, technologies developed by our competitors may render our product candidates uneconomical or obsolete, and we or our collaborators may not be successful in marketing any product candidates we may develop against competitors. The availability of our competitors' products could limit the demand, and the price we are able to charge, for any products that we develop alone or with collaborators.

Our future profitability, if any, depends in part on our and our collaborators' ability to penetrate global markets, where we would be subject to additional regulatory burdens and other risks and uncertainties associated with international operations that could materially adversely affect our business.

Our future profitability, if any, will depend in part on our ability and the ability of our collaborators to commercialize any products that we or our collaborators may develop in markets throughout the world. Commercialization of products in various markets could subject us to risks and uncertainties, including:

- obtaining, on a country-by-country basis, the applicable marketing authorization from the competent regulatory authority;

- the burden of complying with complex and changing regulatory, tax, accounting, labor and other legal requirements in each jurisdiction that we or our collaborators pursue;
- reduced protection for intellectual property rights;
- differing medical and agricultural practices and customs affecting acceptance in the marketplace;
- import or export licensing requirements;
- governmental controls, trade restrictions or changes in tariffs;
- economic weakness, including inflation, or political instability in particular non-U.S. economies and markets;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad;
- longer accounts receivable collection times;
- longer lead times for shipping;
- language barriers;
- foreign currency exchange rate fluctuations;
- foreign reimbursement, pricing and insurance regimes; and
- the interpretation of contractual provisions governed by foreign laws in the event of a contract dispute.

We have limited or no prior experience in these areas, and our collaborators may have limited experience in these areas. Failure to successfully navigate these risks and uncertainties may limit or prevent market penetration for any products that we or our collaborators may develop, which would limit their commercial potential and our revenues.

Product liability lawsuits against us could cause us to incur substantial liabilities and could limit commercialization of any products that we develop alone or with collaborators.

We face an inherent risk of product liability and professional indemnity exposure related to the testing in clinical or field trials of our product candidates. We will face an even greater liability risk if we commercially sell any products that we or our collaborators may develop for human use or consumption. Manufacturing defects, errors in product distribution or storage processes, improper administration or application and known or unknown side effects of product usage may result in liability claims against us or third parties with which we have relationships. These actions could include claims resulting from acts by our collaborators, licensees and subcontractors over which we have little or no control.

For example, our liability could be sought by patients participating in clinical trials for potential therapeutic product candidates as a result of unexpected side effects, improper product administration or the deterioration of a patient's condition, patient injury or even death. Criminal or civil proceedings might be filed against us by patients, regulatory authorities, biopharmaceutical companies and any other third party using or marketing any product candidates or products that we develop alone or with collaborators. On occasion, large judgments have been awarded in class action lawsuits based on products that had unanticipated adverse effects. If we cannot successfully defend ourselves against claims that product candidates or products we develop alone or with collaborators caused harm, we could incur substantial liabilities.

Regardless of merit or eventual outcome, liability claims may result in:

- significant time and costs to defend the related litigation;
- injury to our reputation and significant negative media attention;
- diversion of management's attention from pursuing our strategy;
- withdrawal of clinical trial participants;
- delay or termination of clinical trials;
- decreased demand for any products that we develop alone or with collaborators;
- substantial monetary awards to trial participants or patients;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;

- loss of revenue; and
- the inability to further develop or commercialize any products.

Although the clinical trial process is designed to identify and assess potential side effects, clinical development does not always fully characterize the safety and efficacy profile of a new medicine, and it is always possible that a drug or biologic, even after regulatory approval, may exhibit unforeseen side effects. If our product candidates were to cause adverse side effects during clinical trials or after approval, we may be exposed to substantial liabilities. Physicians and patients may not comply with any warnings that identify known potential adverse effects and patients who should not use our product candidates. If any of our product candidates are approved for commercial sale, we will be highly dependent upon consumer perceptions of us and the safety and quality of such products. We could be adversely affected if we are subject to negative publicity associated with illness or other adverse effects resulting from patients' use or misuse of such products or any similar products distributed by other companies.

Although we maintain product liability insurance coverage, it may not be adequate to cover all liabilities that we may incur. We anticipate that we will need to increase our insurance coverage if we or our collaborators successfully commercialize any products. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liabilities to which we may become subject.

Additional Risks Related to the Identification, Development and Commercialization of Our Therapeutic Product Candidates

The regulatory landscape that will apply to development of therapeutic product candidates by us or our collaborators is rigorous, complex, uncertain and subject to change, which could result in delays or termination of development of such product candidates or unexpected costs in obtaining regulatory approvals.

Regulatory requirements governing products created with genome editing technology or involving gene therapy treatment have changed frequently and will likely continue to change in the future. Approvals by one regulatory agency may not be indicative of what any other regulatory agency may require for approval, and there has historically been substantial, and sometimes uncoordinated, overlap in those responsible for regulation of gene therapy products, cell therapy products and other products created with genome editing technology. For example, in the United States, the FDA has established the Office of Tissues and Advanced Therapies within its Center for Biologics Evaluation and Research, or CBER, to consolidate the review of gene therapy and related products, and the Cellular, Tissues, and Gene Therapies Advisory Committee to advise CBER on its review. Our product candidates will need to meet safety and efficacy standards applicable to any new biologic under the regulatory framework administered by the FDA.

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 subject to the NIH Guidelines are 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. The IBC assesses the safety of the research and identifies any potential risk to public health or the environment, and such review may result in some delay before initiation of a clinical trial. While the NIH Guidelines are not mandatory unless the research in question is being conducted at or sponsored by institutions receiving NIH funding of recombinant or synthetic nucleic acid molecule research, many companies and other institutions not otherwise subject to the NIH Guidelines voluntarily follow them. We are subject to significant regulatory oversight by the FDA, and in addition to the government regulators, the applicable IBC and institutional review board, or IRB, of each institution at which we or our collaborators conduct clinical trials of our product candidates, or a central IRB if appropriate, would need to review and approve the proposed clinical trial.

The same applies in the European Union, or the EU. The European Medicines Agency, or the EMA, has a Committee for Advanced Therapies, or CAT, that is responsible for assessing the quality, safety and efficacy of advanced-therapy medicinal products. Advanced-therapy medical products include gene therapy medicine, somatic-cell therapy medicines and tissue-engineered medicines. The role of the CAT is to prepare a draft opinion on an application for marketing authorization for a gene therapy medicinal product candidate that is submitted to the EMA. In the EU, the development and evaluation of a gene therapy medicinal product must be considered in the context of the relevant EU guidelines. The EMA may issue new guidelines concerning the development and marketing authorization for gene therapy medicinal products and require that we comply with these new guidelines. Similarly complex regulatory environments exist in other jurisdictions in which we might consider seeking regulatory approvals for our product candidates, further complicating the regulatory landscape. As a result, the procedures and standards applied to gene therapy products and cell therapy products may be applied to any of our gene therapy or genome editing product candidates, but that remains uncertain at this point.

The clinical trial requirements of the FDA, the EMA and other regulatory authorities and the criteria these regulators use to evaluate 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 product candidates created with novel genome editing technology such as ours can be more lengthy, rigorous and expensive than the process for other better known or more extensively studied product candidates and technologies. Since we are developing novel treatments for diseases in which there is little clinical experience with new endpoints and methodologies, there is heightened risk that the FDA, the EMA or comparable 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. This may be a particularly significant risk for many of the genetically defined diseases for which we may develop product candidates alone or with collaborators due to small patient populations for those diseases, and designing and executing a rigorous clinical trial with appropriate statistical power is more difficult than with diseases that have larger patient populations. Regulatory agencies administering existing or future regulations or legislation may not allow production and marketing of products utilizing genome editing technology in a timely manner or under technically or commercially feasible conditions. Even if our product candidates obtain required regulatory approvals, such approvals may later be withdrawn as a result of changes in regulations or the interpretation of regulations by applicable regulatory agencies.

Changes in applicable regulatory guidelines may lengthen the regulatory review process for our product candidates, require additional studies or trials, increase development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of such product candidates, or lead to significant post-approval limitations or restrictions. Additionally, adverse developments in clinical trials conducted by others of gene therapy products or products created using genome editing technology, such as products developed through the application of a CRISPR/Cas9 technology, or adverse public perception of the field of genome editing, may cause the FDA, the EMA and other regulatory bodies to revise the requirements for approval of any product candidates we may develop or limit the use of products utilizing genome editing technologies, either of which could materially harm our business. Furthermore, regulatory action or private litigation could result in expenses, delays or other impediments to our research programs or the development or commercialization of current or future product candidates.

As we advance product candidates alone or with collaborators, we will be required to consult with these regulatory and advisory groups and comply with all applicable guidelines, rules and regulations. If we fail to do so, we or our collaborators may be required to delay or terminate development of such product candidates. Delay or failure to obtain, or unexpected costs in obtaining, the regulatory approval necessary to bring a product candidate to market could decrease our ability to generate sufficient product revenue to maintain our business.

We may not be able to file IND applications to commence additional clinical trials on the timelines we expect, and even if we are able to, the FDA may not permit us to proceed.

We plan to submit IND applications to enable us to conduct clinical trials for additional product candidates in the future, and we expect to file IND amendments to enable us to conduct additional clinical trials under existing INDs. We cannot be sure that submission of an IND application or IND amendment will result in us being allowed to proceed with clinical trials, or that, once begun, issues will not arise that could result in the suspension or termination such clinical trials. The manufacturing of allogeneic CAR T cell therapy remains an emerging and evolving field. Accordingly, we expect chemistry, manufacturing and controls-related topics, including product specifications, will be a focus of IND reviews, which may delay receipt of authorization to proceed under INDs. Additionally, even if such regulatory authorities agree with the design and implementation of the clinical trials set forth in an IND or clinical trial application, we cannot guarantee that such regulatory authorities will not change their requirements in the future.

The regulatory approval processes of the FDA and comparable foreign authorities are lengthy, time consuming and inherently unpredictable, and if we are ultimately unable to obtain regulatory approval for our product candidates, our business will be substantially harmed.

We and any collaborators are not permitted to commercialize, market, promote or sell any product candidate in the United States without obtaining marketing approval from the FDA. Foreign regulatory authorities, such as the EMA, impose similar requirements. The time required to obtain approval by the FDA, the EMA and comparable foreign authorities is unpredictable, but typically takes many years following the commencement of clinical trials and depends upon numerous factors, including substantial discretion of the regulatory authorities and sufficient resources at the FDA. In addition, approval policies, regulations or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions. To date, we have not submitted a biologics license application, or BLA, or other marketing authorization application to the FDA or similar drug approval submissions to comparable foreign regulatory authorities for any product candidate. We and any collaborators must complete additional preclinical or nonclinical studies and clinical trials to demonstrate the safety and efficacy of our product candidates in humans to the satisfaction of the regulatory authorities before we will be able to obtain these approvals.

Our product candidates could fail to receive regulatory approval for many reasons, including the following:

- the FDA or comparable foreign regulatory authorities may disagree with the design or implementation of our or our collaborators' clinical trials;
- we or our collaborators may be unable to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that a product candidate is safe and effective for its proposed indication;
- the results of clinical trials may not meet the level of statistical significance required by the FDA or comparable foreign regulatory authorities for approval;
- we or our collaborators may be unable to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;
- the FDA or comparable foreign regulatory authorities may disagree with our or our collaborators' interpretation of data from preclinical studies or clinical trials;
- the data collected from clinical trials of product candidates may not be sufficient to support the submission of a BLA or other submission or to obtain regulatory approval in the United States or elsewhere;
- the FDA or comparable foreign regulatory authorities may fail to approve the manufacturing processes or facilities of third-party manufacturers with which we or our collaborators contract for clinical and commercial supplies;
- the FDA or comparable foreign regulatory authorities may fail to approve the companion diagnostics we may contemplate developing with collaborators; and
- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our or our collaborators' clinical data insufficient for approval.

This lengthy approval process as well as the unpredictability of future clinical trial results may result in our failing to obtain regulatory approval to market our product candidates, which would significantly harm our business, results of operations and prospects.

In addition, even if we were to obtain approval, regulatory authorities may approve any of our product candidates for fewer or more limited indications than we request, may impose significant limitations in the form of narrow indications, warnings, or a Risk Evaluation and Mitigation Strategy, or REMS. Regulatory authorities may not approve the price we or our collaborators intend to charge for products we may develop, may grant approval contingent on the performance of costly post-marketing clinical trials, or may approve a product candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that product candidate. Any of the foregoing scenarios could materially harm the commercial prospects for our product candidates.

Clinical trials are difficult to design and implement, expensive, time-consuming and involve an uncertain outcome, and the inability to successfully and timely conduct clinical trials and obtain regulatory approval for our product candidates would substantially harm our business.

Clinical testing is expensive and usually takes many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process, and product candidates in later stages of clinical trials may fail to show the desired safety and efficacy traits despite having progressed through preclinical studies and initial clinical trials. We have initiated a Phase 1/2a clinical trial in patients with R/R NHL or R/R B-ALL, a Phase 1/2a clinical trial in subjects with NHL, chronic lymphocytic leukemia and small lymphocytic lymphoma, and a Phase 1/2a clinical trial in subjects with R/R multiple myeloma. We do not know whether any current or planned clinical trials will need to be redesigned, recruit and enroll patients on time or be completed on schedule, or at all. Clinical trials have been and may in the future be delayed, suspended or terminated for a variety of reasons, including in connection with:

- the inability to generate sufficient preclinical, toxicology or other *in vivo* or *in vitro* data to support the initiation of clinical trials;
- applicable regulatory authorities disagreeing as to the design or implementation of the clinical trials;
- obtaining regulatory authorization to commence a trial;
- reaching an agreement on acceptable terms with prospective contract research organizations, or CROs, and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- obtaining IRB approval at each site;
- developing and validating the companion diagnostic to be used in a clinical trial, if applicable;

- insufficient or inadequate supply or quality of product candidates or other materials, including identification of lymphocyte donors meeting regulatory standards necessary for use in clinical trials, or delays in sufficiently developing, characterizing or controlling a manufacturing process suitable for clinical trials;
- recruiting and retaining enough suitable patients to participate in a trial;
- having enough patients complete a trial or return for post-treatment follow-up;
- adding a sufficient number of clinical trial sites;
- inspections of clinical trial sites or operations by applicable regulatory authorities, or the imposition of a clinical hold;
- clinical sites deviating from trial protocol or dropping out of a trial;
- the inability to demonstrate the efficacy and benefits of a product candidate;
- discovering that product candidates have unforeseen safety issues, undesirable side effects or other unexpected characteristics;
- addressing patient safety concerns that arise during the course of a trial;
- receiving untimely or unfavorable feedback from applicable regulatory authorities regarding the trial or requests from regulatory authorities to modify the design of a trial;
- non-compliance with applicable regulatory requirements by us or third parties or changes in such regulations or administrative actions;
- suspensions or terminations by IRBs of the institutions at which such trials are being conducted, by the Data Safety Monitoring Board, or DSMB, for such trial or by the FDA or other regulatory authorities due to a number of factors, including those described above;
- third parties being unable or unwilling to satisfy their contractual obligations to us;
- changes in our financial priorities, greater than anticipated costs of completing a trial or our inability to continue funding the trial; or
- unforeseen events, such as natural or manmade disasters, public health emergencies, such as the COVID-19 pandemic, which has and may continue to impact our operations, or other natural catastrophic events.

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. Additionally, we or our collaborators may experience unforeseen events during or resulting from clinical trials that could delay or prevent receipt of marketing approval for or commercialization of product candidates. For example, clinical trials of product candidates may produce negative, inconsistent or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon development programs. Regulators may also revise the requirements for approving the product candidates, or such requirements may not be as we anticipate. If we or our collaborators are required to conduct additional clinical trials or other testing of product candidates beyond those that we or our collaborators currently contemplate, if we or our collaborators are unable to successfully complete clinical trials or other testing of such product candidates, if the results of these trials or tests are not positive or are only modestly positive or if there are safety concerns, we may:

- incur unplanned costs;
- be delayed in obtaining or fail to obtain marketing approval for product candidates;
- obtain marketing approval in some countries and not in others;
- obtain marketing approval for indications or patient populations that are not as broad as intended or desired;
- obtain marketing approval with labeling that includes significant use or distribution restrictions or safety warnings, including boxed warnings;
- be subject to additional post-marketing testing requirements;
- be subject to changes in the way the product is administered;
- have regulatory authorities withdraw or suspend their approval of the product or impose restrictions on its distribution;
- be sued; or
- experience damage to our reputation.

If we or our collaborators experience delays in the commencement or completion of our clinical trials, or if we or our collaborators terminate a clinical trial prior to completion, we may experience increased costs, have difficulty raising capital and/or be required to slow down the development and approval process timelines. Furthermore, the product candidates that are the subject of such trials may never receive regulatory approval, and their commercial prospects and our ability to generate product revenues from them could be impaired or not realized at all.

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 authorities 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 authorities 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 authorities, as the case may be, and may ultimately lead to the denial of marketing approval of one or more of our product candidates.

Any product candidates that we or our collaborators may develop will be novel and may be complex and difficult to manufacture, and if we experience manufacturing problems, it could result in delays in development and commercialization of such product candidates or otherwise harm our business.

Our product candidates involve or will involve novel genome editing technology and will require processing steps that are more complex than those required for most small molecule drugs, resulting in a relatively higher manufacturing cost. Moreover, unlike small molecules, the physical and chemical properties of biologics generally cannot be fully characterized. As a result, assays of the finished product may not be sufficient to ensure that such product will perform in the intended manner. Although we intend to employ multiple steps to control the manufacturing process, we may experience manufacturing issues with any of our product candidates that could cause production interruptions, including contamination, equipment or reagent failure, improper installation or operation of equipment, facility contamination, raw material shortages or contamination, natural disasters, disruption in utility services, human error, disruptions in the operations of our suppliers, inconsistency in cell growth and variability in product characteristics. We may encounter problems achieving adequate quantities and quality of clinical-grade materials that meet FDA, EMA or other comparable applicable standards or specifications with consistent and acceptable production yields and costs. For example, the FDA has required us to conduct testing of our allogeneic CAR T cell product candidates for the presence of certain human viruses prior to release of such products for clinical use. If the FDA concludes that further such viral testing of our product candidates is required and that any lots testing positive may not be used in clinical trials, we may need to produce new clinical trial materials, which could delay our clinical trials and result in higher manufacturing costs. Even minor deviations from normal manufacturing processes could result in reduced production yields, product defects and other supply disruptions. If microbial, viral or other contaminations are discovered in our product candidates or in the manufacturing facilities in which such product candidates are made, such manufacturing facilities may need to be closed for an extended period of time to investigate and remedy the contamination. Our manufacturing process for any allogeneic CAR T cell product candidate that we develop alone or with collaborators will be susceptible to product loss or failure due to the quality of the raw materials, failure of the products to meet specifications, logistical issues associated with the collection of white blood cells, or starting material, from healthy third-party donors, shipping such material to the manufacturing site, ensuring standardized production batch-to-batch in the context of mass production, freezing the manufactured product, shipping the final product globally and infusing patients with such product. 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, delays in initiating or completing clinical trials, product recalls, product liability claims or insufficient inventory.

As product candidates are developed through preclinical to late-stage clinical trials towards approval and commercialization, we expect that various aspects of the development program, such as manufacturing methods, may be altered along the way in an effort to help optimize processes and results. Such changes carry the risk that they will not achieve the intended objectives, and any of these changes could cause our product candidates to perform differently and affect the results of future clinical trials or our reliance on results of trials that have previously been conducted using the product candidate in its previous form. If the manufacturing process is changed during the course of product development, we or our collaborators may be required to repeat some or all of the previously conducted trials or conduct additional bridging trials, which could increase our costs and delay or impede our ability to obtain marketing approval.

We expect our manufacturing strategy for one or more of our product candidates may involve the use of contract manufacturing organizations, or CMOs, as well as our newly opened manufacturing facility, MCAT. The facilities used by us and our contract manufacturers to manufacture therapeutic product candidates must be approved by the FDA pursuant to inspections that will be conducted after we submit our BLA to the FDA. We do not control the manufacturing process of our contract manufacturers and are dependent on their compliance with cGMP for their manufacture of our product candidates. We may establish multiple manufacturing facilities as we expand our commercial footprint to multiple geographies, which will be costly and time consuming and may lead to regulatory delays. Even if we are successful, our manufacturing capabilities could be affected by cost-overruns, potential problems

with scale-out, process reproducibility, stability issues, lot inconsistency, timely availability of reagents or raw materials, unexpected delays, equipment failures, labor shortages, natural disasters, utility failures, regulatory issues and other factors that could prevent us from realizing the intended benefits of our manufacturing strategy and have a material adverse effect on our business.

The FDA, the EMA and other foreign regulatory authorities may require us to submit samples of any lot of any product that may receive approval 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 relevant 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 or our collaborators to delay product launches or clinical trials, which could be costly to us and otherwise harm our business. Problems in our manufacturing process also could restrict our or our collaborators' ability to meet market demand for products.

Any problems in our manufacturing process or facilities could make us a less attractive collaborator for potential partners, including larger pharmaceutical companies and academic research institutions, which could limit our access to additional attractive development opportunities.

We will rely on donors of T cells to manufacture product candidates from our allogeneic CAR T immunotherapy platform, and if we do not obtain an adequate supply of T cells from qualified donors, development of those product candidates may be adversely impacted.

We are developing a pipeline of allogeneic T cell product candidates that are engineered from healthy donor T cells, which vary in type and quality. This variability in type and quality of a donor's T cells makes producing standardized product candidates more difficult and makes the development and commercialization pathway of those product candidates more uncertain. We have developed a screening process designed to enhance the quality and consistency of T cells used in the manufacture of our CAR T cell product candidates. If we are unable to identify and obtain T cells from donors that satisfy our criteria in sufficient quantity, to obtain such cells in a timely manner or to address variability in donor T cells, development of our CAR T cell product candidates may be delayed or there may be inconsistencies in the product candidates we produce, which could negatively impact development of such product candidates, harm our reputation and adversely impact our business and prospects.

Failure to achieve operating efficiencies from MCAT may require us to devote additional resources and management time to manufacturing operations and may delay our product development timelines.

We have leased approximately 33,800 square feet of space for MCAT at a location approximately seven miles from our headquarters in Durham, North Carolina. We use this manufacturing center to create clinical trial material for certain of our current and planned clinical trials. We may not experience the anticipated operating efficiencies in our own manufacturing. Any delays in manufacturing may disrupt or delay the supply of our product candidates if we have not maintained a sufficient back-up supply of such product candidates through third-party manufacturers. Moreover, changing manufacturing facilities may also require that we or our collaborators conduct additional studies, make notifications to regulatory authorities, make additional filings to regulatory authorities, and obtain regulatory authority approval for the new facilities, which may be delayed or which we may never receive. We are also required to comply with the FDA's and applicable foreign regulatory authorities' cGMP requirements for the production of product candidates for clinical trials and, if approved, commercial supply, and will be subject to FDA and comparable foreign regulatory authority inspection. These requirements include the qualification and validation of our manufacturing equipment and processes. We may not be able to develop, acquire or maintain the internal expertise and resources necessary for compliance with these requirements. If we fail to achieve the operating efficiencies that we anticipate, our manufacturing and operating costs may be greater than expected, which could have a material adverse impact on our operating results.

We also may encounter problems hiring and retaining the experienced scientific, quality-control and manufacturing personnel needed to operate our manufacturing processes. If we experience unanticipated employee shortage or turnover in any of these areas, we may not be able to effectively manage our ongoing manufacturing operations and we may not achieve the operating efficiencies that we anticipate from the new facility, which may negatively affect our product development timeline or result in difficulties in maintaining compliance with applicable regulatory requirements.

Any such problems could result in the delay, prevention or impairment of clinical development and commercialization of our product candidates.

Any delays or difficulties in our or our collaborators ability to enroll patients in clinical trials, could delay or prevent receipt of regulatory approvals.

We or our collaborators may not be able to initiate or continue clinical trials on a timely basis or at all for any product candidates we or our collaborators identify or develop if we or our collaborators are unable to locate and enroll a sufficient number of eligible

patients to participate in the trials as required by applicable regulations or as needed to provide appropriate statistical power for a given trial. Additionally, some of our competitors may have ongoing clinical trials for product candidates that would treat the same indications as one or more of our product candidates, and patients who would otherwise be eligible for our clinical trials may instead enroll in our competitors' clinical trials.

Patient enrollment may also be affected by many factors, including:

- severity and difficulty of diagnosing of the disease under investigation;
- the difficulty in recruiting and/or identifying eligible patients suffering from rare diseases being evaluated under our trials;
- size of the patient population and process for identifying subjects;
- eligibility and exclusion criteria for the trial in question, including unforeseen requirements by the FDA or other regulatory authorities that we restrict one or more entry criteria for the study for safety reasons;
- our or our collaborators' ability to recruit clinical trial investigators with the appropriate competencies and experience;
- design of the trial protocol;
- availability and efficacy of approved medications or therapies, or other clinical trials, for the disease or condition under investigation;
- perceived risks and benefits of the product candidate under trial or testing, or of the application of genome editing to human indications;
- availability of genetic testing for potential patients;
- efforts to facilitate timely enrollment in clinical trials;
- patient referral practices of physicians;
- ability to obtain and maintain subject consent;
- risk that enrolled subjects will drop out before completion of the trial;
- ability to monitor patients adequately during and after treatment;
- proximity and availability of clinical trial sites for prospective patients; and
- unforeseen events, such as natural or manmade disasters, public health emergencies, such as the COVID-19 pandemic which has and may continue to impact our operations, or other natural catastrophic events.

We expect that some of our product candidates will focus on rare genetically defined diseases with limited patient pools from which to draw for enrollment in clinical trials. The eligibility criteria of our clinical trials will further limit the pool of available trial participants. In addition to the factors identified above, patient enrollment in any clinical trials we or our collaborators may conduct may be adversely impacted by any negative outcomes our competitors may experience, including adverse side effects, clinical data showing inadequate efficacy or failures to obtain regulatory approval.

Furthermore, our or our collaborators' ability to successfully initiate, enroll and conduct a clinical trial outside the United States is subject to numerous additional risks, including:

- difficulty in establishing or managing relationships with CROs and physicians;
- differing standards for the conduct of clinical trials;
- differing standards of care for patients with a particular disease;
- an inability to locate qualified local consultants, physicians and partners; and
- the potential burden of complying with a variety of foreign laws, medical standards and regulatory requirements, including the regulation of pharmaceutical and biotechnology products and treatments.

Enrollment delays in clinical trials, including those due to the COVID-19 pandemic, may result in increased development costs for any of our product candidates, which may cause the value of our company to decline and limit our ability to obtain additional financing. If we or our collaborators have difficulty enrolling a sufficient number of patients to conduct clinical trials as planned, we may need to delay, limit or terminate ongoing or planned clinical trials, any of which may have an adverse effect on our results of operations and prospects.

Results of preclinical studies and early clinical trials of product candidates may not be predictive of results of later studies or trials. Our product candidates may not have favorable results in later clinical trials, if any, or receive regulatory approval.

Preclinical and clinical drug development is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the preclinical study or clinical trial process. Despite promising preclinical or clinical results, any product candidate can unexpectedly fail at any stage of preclinical or clinical development. The historical failure rate for product candidates in our industry is high.

The results from preclinical studies or early clinical trials of a product candidate may not be predictive of the results from later preclinical studies or clinical trials, and interim results of a clinical trial are not necessarily indicative of final results. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy characteristics despite having progressed through preclinical studies and initial clinical trials. Many companies in the biopharmaceutical and biotechnology industries have suffered significant setbacks at later stages of development after achieving positive results in early stages of development, and we may face similar setbacks. These setbacks have been caused by, among other things, preclinical findings made while clinical trials were underway or safety or efficacy observations made in clinical trials, including previously unreported adverse events. Moreover, non-clinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that believed their product candidates performed satisfactorily in preclinical studies and clinical trials nonetheless failed to obtain regulatory approval. With the exception of our allogeneic anti-CD19, anti-CD20 and anti-BCMA CAR T product candidates, which have undergone limited testing in humans to date, our gene editing technology and our product candidates have never undergone testing in humans and have only been tested in a limited manner in animals, and results from animal studies may not be predictive of clinical trial results. Even if product candidates progress to clinical trials, these product candidates may fail to show the safety and efficacy in clinical development required to obtain regulatory approval, despite the observation of positive results in animal studies. Our or our collaborators' failure to replicate positive results from early research programs and preclinical or greenhouse studies may prevent us from further developing and commercializing those or other product candidates, which would limit our potential to generate revenues from them and harm our business and prospects.

For the foregoing reasons, we cannot be certain that any ongoing or future preclinical studies or clinical trials will be successful. Any safety or efficacy concerns observed in any one of our preclinical studies or clinical trials in a targeted area could limit the prospects for regulatory approval of product candidates in that and other areas, which could have a material adverse effect on our business and prospects.

Interim "top-line" and initial data from studies or trials that we announce or publish from time to time may change as more data become available and are subject to audit and verification procedures that could result in material changes in the final data.

From time to time, we may publish initial data or interim "top-line" data from preclinical or greenhouse studies or clinical or field trials. For example, we recently reported initial results from our ongoing Phase 1/2a clinical trial of PBCAR0191. Interim data are subject to the risk that one or more of the outcomes may materially change as more data become available. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the top-line results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Initial or "top-line" data also remain subject to audit and verification procedures that may result in the final data being materially different from these initial data we previously published. As a result, interim and initial data should be viewed with caution until the final data are available. Additionally, 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. Adverse differences between initial or interim data and final data could significantly harm our business prospects.

Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular product candidate or product and our company in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is the material or otherwise appropriate information to include in our disclosure. Any information we determine not to disclose may ultimately be deemed significant by you or others with respect to future decisions, conclusions, views, activities or otherwise regarding a particular product candidate or our business. If the top-line data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, product candidates may be harmed, which could significantly harm our business prospects.

Our product candidates may not work as intended or cause undesirable side effects that, could hinder or prevent receipt of regulatory approval or realization of commercial potential for them or our other product candidates and substantially harm our business.

Our product candidates may be associated with off-target editing or other serious adverse events, undesirable side effects or unexpected characteristics. Results of clinical trials could reveal severe or recurring side effects, toxicities or unexpected events, including death. Off-target cuts could lead to disruption of a gene or a genetic regulatory sequence at an unintended site in the DNA. In those instances where we also provide a segment of DNA, it is possible that following off-target cut events, such DNA could be integrated into the genome at an unintended site, potentially disrupting another important gene or genomic element. There may also be delayed adverse events following exposure to therapeutics made with genome editing technologies due to persistent biologic activity of the genetic material or other components of products used to carry the genetic material. In addition to serious adverse events or side effects caused by product candidates we develop alone or with collaborators, the administration process or related procedures may also cause undesirable side effects. For example, one NHL patient in our Phase 1/2a clinical trial who was treated with PBCAR0191 and eLD suffered episodes of sepsis, which resulted in a fatal outcome. Further, any side effects may not be appropriately recognized or managed by the treating medical staff. We or our collaborators expect to have to educate medical personnel using any product candidates we may develop to understand the side effect profiles for our clinical trials and upon any commercialization of such product candidates. Inadequate recognition or management of the potential side effects of such product candidates could result in patient injury or death.

If any such events occur, clinical trials or commercial distribution of any product candidates or products we develop alone or with collaborators could be suspended or terminated, and our business and reputation could suffer substantial harm. Treatment-related side effects could affect patient recruitment and the ability of enrolled patients to complete the trial or result in potential liability claims. Regulatory authorities could order us or our collaborators to cease further development of, deny approval of or require us to cease selling any product candidates or products for any or all targeted indications. If we or our collaborators elect, or are required, to delay, suspend or terminate any clinical trial or commercialization efforts, the commercial prospects of such product candidates or products may be harmed, and our ability to generate product revenues from them or other product candidates that we develop may be delayed or eliminated.

Additionally, if we successfully develop a product candidate alone or with collaborators and it receives marketing approval, the FDA could require us to adopt a REMS to ensure that the benefits of treatment with such product candidate outweigh the risks for each potential patient, which may include, among other things, a communication plan to health care practitioners, patient education, extensive patient monitoring or distribution systems and processes that are highly controlled, restrictive and more costly than what is typical for the industry. We or our collaborators may also be required to adopt a REMS or engage in similar actions, such as patient education, certification of health care professionals or specific monitoring, if we or others later identify undesirable side effects caused by any product that we develop alone or with collaborators. Such identification could also have several additional significant negative consequences, such as:

- regulatory authorities may suspend, withdraw or limit approvals of such product, or seek an injunction against its manufacture or distribution;
- regulatory authorities may require additional warnings on the label, including “boxed” warnings, or issue safety alerts, Dear Healthcare Provider letters, press releases or other communications containing warnings or other safety information about the product;
- we may be required to create a medication guide outlining the risks of such side effects for distribution to patients;
- we may be required to change the way a product is administered or conduct additional trials;
- the product may become less competitive;
- we or our collaborators may decide to remove the product from the marketplace;
- we may be subject to fines, injunctions or the imposition of civil or criminal penalties;
- we could be sued and be held liable for harm caused to patients; and
- our reputation may suffer.

Any of these events could prevent us or our collaborators from achieving or maintaining market acceptance of any potential product, or otherwise have a negative impact on our business.

We are subject to federal, state and non-U.S. healthcare laws and regulations relating to our business, and could face substantial penalties if we are determined not to have fully complied with such laws, which would have an adverse impact on our business.

Our business operations, as well as our current and anticipated future arrangements with investigators, healthcare professionals, consultants, third-party payors, customers and patients, expose or will expose us to broadly applicable foreign, federal, and state fraud and abuse and other healthcare laws and regulations. These laws constrain the business or financial arrangements and relationships through which we conduct our operations, including how we research, market, sell and distribute any potential products for which we may obtain marketing approval. Such laws include:

- the U.S. federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under a U.S. healthcare program such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the U.S. federal Anti-Kickback Statute or specific intent to violate it in order to have committed a violation;
- U.S. federal civil and criminal false claims laws, including the civil False Claims Act, which can be enforced through civil whistleblower or qui tam actions, and civil monetary penalties laws, prohibits, among other things, individuals and entities from knowingly presenting, or causing to be presented, to the U.S. government, claims for payment or approval that are false or fraudulent, knowingly making, using or causing to be made or used, a false record or statement material to a false or fraudulent claim, or from knowingly making a false statement to avoid, decrease or conceal an obligation to pay money to the U.S. government. In addition, the government may assert that a claim including items or services resulting from a violation of the U.S. federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act;
- the U.S. Health Insurance Portability and Accountability Act of 1996, or HIPAA, which imposes criminal and civil liability for, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private third-party payors, or knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement, in connection with the delivery of, or payment for, healthcare benefits, items or services. Similar to the U.S. 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 U.S. Physician Payments Sunshine Act, which requires certain manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report annually to CMS information related to payments or other "transfers of value" made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain other health care professionals beginning in 2022, and teaching hospitals, and requires applicable manufacturers and group purchasing organizations to report annually to the Centers for Medicare and Medicaid Services, or CMS, ownership and investment interests held by the physicians described above and their immediate family members; and
- analogous state and non-U.S. laws and regulations, such as state anti-kickback and anti-corruption and false claims laws, which may apply to our business practices, including, but not limited to, research, distribution, sales and marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers, or by the patients themselves; state laws and non-U.S. laws and regulations that require pharmaceutical and device companies to comply with the industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the U.S. government or foreign governmental authorities, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state and local laws and regulations and non-U.S. laws and regulations that require manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures and pricing information; state and local laws and non-U.S. laws and regulations which require the registration of pharmaceutical sales representatives.

Efforts to ensure that our current and future business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities may conclude that our business practices, including our relationships with certain physicians, some of whom are compensated in the form of stock options for consulting services provided, do not comply with current or future statutes, regulations, agency guidance or case law involving applicable healthcare laws. If our operations are found to be in violation of any of these or any other health regulatory laws that may apply to us, we may be subject to significant penalties, including the imposition of significant civil, criminal and administrative penalties, damages, monetary fines, disgorgement, individual imprisonment, possible exclusion from participation in Medicare, Medicaid and other U.S. or foreign healthcare programs, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, 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. Defending against any such actions can be costly, 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 above occur, it could adversely affect our ability to operate our business and our results of operations.

Actual or perceived failures to comply with applicable data protection, privacy and security laws, regulations, standards and other requirements, and the increasing use of social media, could adversely affect our business, results of operations, and financial condition.

The global data protection landscape is rapidly evolving, and we are or may become subject to numerous state, federal and foreign laws, requirements and regulations governing the collection, use, disclosure, retention, and security of personal data, such as information that we may collect in connection with clinical trials in the U.S. and abroad. Implementation standards and enforcement practices are likely to remain uncertain for the foreseeable future, and we cannot yet determine the impact future laws, regulations, standards, or perception of their requirements may have on our business. This evolution may create uncertainty in our business, affect our ability to operate in certain jurisdictions or to collect, store, transfer use and share personal information, necessitate the acceptance of more onerous obligations in our contracts, result in liability or impose additional costs on us. The cost of compliance with these laws, regulations and standards can be high and is likely to increase in the future. Any failure or perceived failure by us to comply with federal, state or foreign laws or regulation, our internal policies and procedures or our contracts governing our processing of personal information could result in negative publicity, government investigations and enforcement actions, claims by third parties and damage to our reputation, any of which could have a material adverse effect on our operations, financial performance and business.

As our operations and business grow, we may become subject to or affected by new or additional data protection laws and regulations and face increased scrutiny or attention from regulatory authorities. In the U.S., HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and their implementing regulations, imposes, among other things, certain standards relating to the privacy, security, transmission and breach reporting of individually identifiable health information on covered entities (defined as health plans, health care clearinghouses and certain health care providers) and their respective business associates, individuals or entities that create, receive, maintain or transmit protected health information in connection with providing a service for or on behalf of a covered entity. HIPAA mandates the reporting of certain breaches of health information to HHS, affected individuals and if the breach is large enough, the media. Entities that are found to be in violation of HIPAA as the result of a breach of unsecured protected health information, a complaint about privacy practices or an audit by HHS, may be subject to significant civil, criminal and administrative fines and penalties and/or additional reporting and oversight obligations if required to enter into a resolution agreement and corrective action plan with HHS to settle allegations of HIPAA non-compliance. Even when HIPAA does not apply, according to the Federal Trade Commission or the FTC, failing to take appropriate steps to keep consumers' personal information secure constitutes unfair acts or practices in or affecting commerce in violation of Section 5(a) of the Federal Trade Commission Act. The FTC expects a company's data security measures to be reasonable and appropriate in light of the sensitivity and volume of consumer information it holds, the size and complexity of its business, and the cost of available tools to improve security and reduce vulnerabilities. Individually identifiable health information is considered sensitive data that merits stronger safeguards.

Certain states have also adopted comparable privacy and security laws and regulations, some of which may be more stringent than HIPAA. Such laws and regulations will be subject to interpretation by various courts and other governmental authorities, thus creating potentially complex compliance issues for us and our future customers and strategic partners. In addition, California recently enacted the CCPA, which went into effect on January 1, 2020. The CCPA creates individual privacy rights for California consumers and increases the privacy and security obligations of entities handling certain personal information. The CCPA provides for civil penalties for violations, as well as a private right of action for data breaches that is expected to increase data breach litigation. Further, the CPRA, recently passed in California. The CPRA will impose additional data protection obligations on covered businesses, including additional consumer rights processes, limitations on data uses, new audit requirements for higher risk data, and opt outs for certain uses of sensitive data. It will also create a new California data protection agency authorized to issue substantive regulations and could result in increased privacy and information security enforcement. The majority of the CPRA provisions are expected to go into effect on January 1, 2023. The CCPA, and the CPRA, may increase our compliance costs and potential liability, and many similar laws have been proposed at the federal level and in other states. In the event that we are subject to or affected by HIPAA, the CCPA, the CPRA or other domestic privacy and data protection laws, any liability from failure to comply with the requirements of these laws could adversely affect our financial condition.

In Europe, the GDPR, went into effect in May 2018 and introduces strict requirements for processing the personal data of individuals within the EEA. Companies that must comply with the GDPR face increased compliance obligations and risk, including more robust regulatory enforcement of data protection requirements. From January 1, 2021 we are subject to compliance with the GDPR and the UK GDPR, which, together with the amended UK Data Protection Act 2018, retains the GDPR in UK national law. The UK GDPR mirrors the fines under the GDPR, i.e., fines up to the greater of €20 million/ £17 million or 4% of global turnover. The relationship between the UK and the EU in relation to certain aspects of data protection law remains unclear, and it is unclear how UK data protection laws and regulations will develop in the medium to longer term, and how data transfers between EU member states will be regulated in the long run. Currently there is a four- to six-month grace period agreed in the EU and UK Trade and Cooperation Agreement, ending June 30, 2021 at the latest, whilst the parties discuss an adequacy decision. However, it is not clear whether (and when) an adequacy decision may be granted by the European Commission enabling data transfers from EU member states to the UK long term without additional measures. These changes will lead to additional costs and increase our overall risk exposure.

Recent legal developments in Europe have created complexity and uncertainty regarding transfers of personal data from the EEA and the UK to the U.S. Most recently, on July 16, 2020, the Court of Justice of the European Union, or the CJEU, invalidated the EU-US Privacy Shield Framework, the Privacy Shield, under which personal data could be transferred from the EEA to US entities who had self-certified under the Privacy Shield scheme. While the CJEU upheld the adequacy of the standard contractual clauses (a standard form of contract approved by the European Commission as an adequate personal data transfer mechanism, and potential alternative to the Privacy Shield), it made clear that reliance on them alone may not necessarily be sufficient in all circumstances. Use of the standard contractual clauses must now be assessed on a case-by-case basis taking into account the legal regime applicable in the destination country, in particular applicable surveillance laws and rights of individuals and additional measures and/or contractual provisions may need to be put in place, however, the nature of these additional measures is currently uncertain. The CJEU went on to state that if a competent supervisory authority believes that the standard contractual clauses cannot be complied with in the destination country and the required level of protection cannot be secured by other means, such supervisory authority is under an obligation to suspend or prohibit that transfer.

These recent developments may require us to review and amend the legal mechanisms by which we make and/ or receive personal data transfers to/ in the U.S. As supervisory authorities issue further guidance on personal data export mechanisms, including circumstances where the standard contractual clauses cannot be used, and/or start taking enforcement action, we could suffer additional costs, complaints and/or regulatory investigations or fines, and/or if we are otherwise unable to transfer personal data between and among countries and regions in which we operate, it could affect the manner in which we provide our services, the geographical location or segregation of our relevant systems and operations, and could adversely affect our financial results.

Despite our efforts to monitor evolving social media communication guidelines and comply with applicable rules, there is risk that the use of social media by us or our employees to communicate about our product candidates or business may cause us to be found in violation of applicable requirements. In addition, our employees may knowingly or inadvertently make use of social media in ways that may not comply with our internal policies or other legal or contractual requirements, which may give rise to liability, lead to the loss of trade secrets or other intellectual property, or result in public exposure of personal information of our employees, clinical trial patients, customers and others. Our potential patient population may also be active on social media and use these platforms to comment on the effectiveness of, or adverse experiences with, our product candidates. Negative posts or comments about us or our product candidates on social media could seriously damage our reputation, brand image and goodwill.

Although we work to comply with applicable laws, regulations and standards, our contractual obligations and other legal obligations, these requirements are evolving and may be modified, interpreted and applied in an inconsistent manner from one jurisdiction to another, and may conflict with one another or other legal obligations with which we must comply. Any failure or perceived failure by us or our employees, representatives, contractors, consultants, CROs, collaborators, or other third parties to comply with such requirements or adequately address privacy and security concerns, even if unfounded, could result in additional cost and liability to us, damage our reputation, and adversely affect our business and results of operations.

We have received orphan drug designation for PBCAR0191 for the treatment of ALL and mantle cell lymphoma, or MCL, PBCAR20A for the treatment of MCL, and PBCAR269A for the treatment of multiple myeloma, and we may seek orphan drug designation for some or all of our other product candidates, but we may be unable to obtain such designations or to maintain the benefits associated with orphan drug designation, which may negatively impact our ability to develop or obtain regulatory approval for such product candidates and may reduce our revenue if we obtain such approval.

We may seek orphan drug designation for some or all of our product candidates in specific orphan indications in which there is a medically plausible basis for the use of these products. Under the Orphan Drug Act, the FDA may grant orphan designation to a drug or biologic intended to treat a rare disease or condition, defined as a disease or condition with a patient population of fewer than 200,000 in the United States, or a patient population greater than 200,000 in the United States when there is no reasonable expectation that the cost of developing and making available the drug or biologic in the United States will be recovered from sales in the United States for that drug or biologic. Orphan drug designation must be requested before submitting a biologics license application, 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. Although we may seek orphan product designation for some or all of our other product candidates, we may never receive such designations.

If a product that has orphan drug designation subsequently receives the first FDA approval for a particular active ingredient 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 a BLA, to market the same biologic for the same indication for seven years, except in limited circumstances such as a showing of clinical superiority to the product with orphan product exclusivity or if FDA finds that the holder of the orphan drug exclusivity has not shown that it can ensure 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. Even if we or our collaborators obtain orphan drug designation for a product candidate, we may not be the first to obtain marketing approval for any particular orphan indication due to the uncertainties associated with developing pharmaceutical products. Exclusive marketing rights in the United States may be limited if we or our collaborators 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 or if the manufacturer is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition. Further, even if a product obtains orphan drug exclusivity, that exclusivity may not effectively protect the product from competition because different drugs with different active moieties can be approved for the same condition. Even after an orphan drug is approved, the FDA can subsequently approve the same drug with the same active moiety for the same condition if the FDA concludes that the later drug is safer, more effective, or makes a major contribution to patient care. Furthermore, the FDA can waive orphan exclusivity if we or our collaborators are unable to manufacture sufficient supply of the product.

Similarly, in the EU, a medicinal product may receive orphan designation under Article 3 of Regulation (EC) 141/2000. This applies to products that are intended for a life-threatening or chronically debilitating condition and either (1) such condition affects not more than five in 10,000 persons in the EU when the application is made, or (2) the product, without the benefits derived from orphan status, would be unlikely to generate sufficient returns in the EU to justify the necessary investment. Moreover, in order to obtain orphan designation in the EU it is necessary to demonstrate that there exists 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 will be of significant benefit to those affected by the condition. In the EU, orphan medicinal products are eligible for financial incentives such as reduction of fees or fee waivers and applicants can benefit from specific regulatory assistance and scientific advice. Products receiving orphan designation in the EU can receive 10 years of market exclusivity, during which time no similar medicinal product for the same indication may be placed on the market. An orphan product can also obtain an additional two years of market exclusivity in the EU for pediatric studies. However, the 10-year market exclusivity may be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for orphan designation—for example, if the product is sufficiently profitable not to justify maintenance of market exclusivity. Additionally, marketing authorization may be granted to a similar product for the same indication at any time if:

- the second applicant can establish that its product, although similar, is safer, more effective or otherwise clinically superior;
- the first applicant consents to a second orphan medicinal product application; or
- the first applicant cannot supply enough orphan medicinal product.

If we or our collaborators do not receive or maintain orphan drug designation for product candidates for which we seek such designation, it could limit our ability to realize revenues from such product candidates.

We have received and may continue to seek fast track designation, and may seek breakthrough therapy designation, Regenerative Medicine Advanced Therapy, or RMAT, designation, or priority review from the FDA or access to the PRIME scheme from the EMA for some or all of our product candidates, but we may not receive such designations, and even if we do, it may not lead to a faster development or regulatory review or approval process, and will not increase the likelihood that such product candidates will receive marketing approval.

We have received fast track designation for PBCAR0191 for the treatment of B-ALL as well as PBCAR269A for R/R multiple myeloma. We may continue to seek fast track designation and may also seek breakthrough therapy designation, Regenerative Medicine Advanced Therapy, or RMAT, designation or priority review from the FDA, or access to the PRIME scheme from the EMA for some or all of our product candidates. If a drug is intended for the treatment of a serious or life-threatening condition or disease, and nonclinical or clinical data demonstrate the potential to address an unmet medical need, the product may qualify for FDA fast track designation, for which sponsors must apply. The FDA has broad discretion whether or not to grant this designation. If granted, fast track designation makes a drug eligible for more frequent interactions with FDA to discuss the development plan and clinical trial design, as well as rolling review of the application, which means that the company can submit completed sections of its marketing

application for review prior to completion of the entire submission. Products with fast track designation may also be eligible for accelerated approval and priority review, if the relevant criteria are met.

Breakthrough therapy designation is intended to expedite the development and review of product candidates that 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 the same potential benefits as a fast track designation, with more intensive FDA guidance on an efficient development program and an organizational commitment at FDA involving senior managers.

A company may also request RMAT designation of its product candidate, which designation may be granted if the drug meets the following criteria: (1) 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; (2) it is intended to treat, modify, reverse, or cure a serious or life-threatening disease or condition; and (3) 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 FDA to discuss the development plan for the product candidate, and potential 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 studies, 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.

PRIME is a scheme provided by the EMA to enhance support for the development of medicines that target an unmet medical need. To qualify for PRIME, product candidates require early clinical evidence that the therapy has the potential to offer a therapeutic advantage over existing treatments or benefits patients without treatment options. Among the benefits of PRIME are the appointment of a rapporteur to provide continuous support and help build knowledge ahead of a marketing authorization application, early dialogue and scientific advice at key development milestones, and the potential to qualify products for accelerated review earlier in the application process.

Based on legislation adopted late in 2007, the EMA established an additional regulatory designation for products classified as an advanced therapy medicinal product (ATMP). The ATMP classification offers sponsors a variety of benefits similar to those associated with the PRIME scheme, including scientific and regulatory guidance, additional opportunities for dialogue with regulators, and presubmission review and certification of the CMC and nonclinical data proposed for submission in a forthcoming MA applications for micro-, small-, or medium-sized enterprises. To qualify for this designation, product candidates intended for human use must be based on gene therapy, somatic cell therapy, or tissue engineered therapy (i.e., engineered cells or tissues intended to regenerate, replace or repair human tissue).

There is no assurance that we will obtain additional fast track designation, or that we will obtain breakthrough therapy designation, RMAT designation or access to PRIME or ATMP for any of our product candidates. Fast track designation, breakthrough therapy designation, RMAT designation and PRIME and ATMP eligibility do not change the standards for product approval, and there is no assurance that any 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 fast track designation, breakthrough therapy designation, RMAT designation or PRIME or ATMP eligibility. Additionally, fast track designation, breakthrough therapy designation, RMAT designation and access to PRIME or ATMP can each be revoked if the criteria for eligibility cease to be met as clinical data emerges.

If the product candidates that we or our collaborators may develop receive regulatory approval in the United States or another jurisdiction, they may never receive approval in other jurisdictions, which would limit market opportunities for such product candidate and adversely affect our business.

Approval of a product candidate in the United States by the FDA or by the requisite regulatory agencies in any other jurisdiction does not ensure approval of such product candidate by regulatory authorities in other countries or jurisdictions. The approval process varies among countries and may limit our or our collaborators' ability to develop, manufacture, promote and sell product candidates internationally. Failure to obtain marketing approval in international jurisdictions would prevent the product candidates from being marketed outside of the jurisdictions in which regulatory approvals have been received. In order to market and sell product candidates in the EU and many other jurisdictions, we and our collaborators must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and may involve additional preclinical studies or clinical trials both before and after approval. In many countries, any product candidate for human use must be approved for reimbursement before it can be approved for sale in that country. In some cases, the intended price for such product is also subject to

approval. Further, while regulatory approval of a product candidate in one country does not ensure approval in any other country, a failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory approval process in others. If we or our collaborators fail to comply with the regulatory requirements in international markets or to obtain all required marketing approvals, the target market for a particular potential product will be reduced, which would limit our ability to realize the full market potential for the product and adversely affect our business.

Current and future legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize any product candidates we or our collaborators develop and may adversely affect the prices for such product candidates.

In the United States and certain non-U.S. jurisdictions, there have been, and we expect there will continue to be, a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could, among other things, prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our or our collaborators' ability to profitably sell any product candidates that obtain marketing approval.

For example, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, collectively the Affordable Care Act, was enacted in the United States. Among the provisions of the Affordable Care Act of importance to our product candidates, the Affordable Care Act established an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents; increased the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program, extended manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations, expanded eligibility criteria for Medicaid programs, expanded the entities eligible for discounts under the Public Health program, addressed 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, created a new Medicare Part D coverage gap discount program, in which manufacturers must now agree to offer 70% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D, and created a licensure framework for follow-on biologic products.

Since its enactment, there have been judicial and Congressional challenges to certain aspects of the Affordable Care Act, as well as efforts by the Trump administration to repeal or replace certain aspects of the Affordable Care Act and we expect such challenges and amendments to continue. On December 14, 2018, a U.S. District Court Judge in the Northern District of Texas, or Texas District Court Judge, ruled that the entire Affordable Care Act is invalid based primarily on the fact that the TCJA enacted on December 22, 2017, repealed the tax-based shared responsibility payment imposed by the Affordable Care Act, on certain individuals who fail to maintain qualifying health coverage for all or part of a year, which is commonly referred to as the "individual mandate." On December 18, 2019, the U.S. Court of Appeals for the 5th Circuit upheld the District Court's decision that the individual mandate was unconstitutional but remanded the case back to the District Court to determine whether the remaining provisions of the Affordable Care Act are invalid as well. The case is currently being reviewed by the U.S. Supreme Court, although it is unclear when or how the Supreme Court will rule. It is also unclear how other efforts, if any, to challenge, repeal or replace the Affordable Care Act will impact the law or our business.

In addition, other legislative changes have been proposed and adopted since the Affordable Care Act was enacted. On August 2, 2011, the Budget Control Act of 2011 was signed into law, which, among other things, included reductions to Medicare payments to providers of 2% per fiscal year, which went into effect on April 1, 2013 and, due to subsequent legislative amendments to the statute, will remain in effect through 2030, with the exception of a temporary suspension from May 1, 2020 through March 31, 2021, unless additional Congressional action is taken. On January 2, 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, reduced Medicare payments to several providers, including hospitals, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

Further, there has been heightened governmental scrutiny recently over pharmaceutical pricing practices in light of the rising cost of prescription drugs and biologics. Such scrutiny has resulted in several Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies, rebates and price negotiation for pharmaceutical products. The probability of success of any previously announced policies under the Trump administration and their impact on the United States prescription drug marketplace is unknown, particularly in light of the new Biden administration. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical product and medical device pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and medical devices to purchase and which suppliers will be included in their prescription drug and other healthcare programs.

Additionally, on May 30, 2018, the Trickett Wendler, Frank Mongiello, Jordan McLinn, and Matthew Bellina Right to Try Act of 2017, or the Right to Try Act, was signed into law. The law, among other things, provides a framework for certain patients with life-threatening diseases or conditions 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 drug manufacturer to make its drug products available to eligible patients as a result of the Right to Try Act.

We expect that the Affordable Care Act, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria, new payment methodologies and in additional downward pressure on the price that we or our collaborators may receive for any approved or cleared product. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we or our collaborators are slow or unable to adapt to new requirements or policies, or if we or our collaborators are not able to maintain regulatory compliance, any of our product candidates may lose any regulatory approval that may have been obtained and we may not achieve or sustain profitability, which would adversely affect our business.

Even if we obtain regulatory approval for any products that we develop alone or with collaborators, such products will remain subject to ongoing regulatory requirements, which may result in significant additional expense.

Even if products we develop alone or with collaborators receive regulatory approval, they will be subject to ongoing regulatory requirements for manufacturing, labeling, packaging, distribution, storage, advertising, promotion, sampling, record-keeping and submission of safety and other post-market information, among other things. Any regulatory approvals received for such products may also be subject to limitations on the approved indicated uses for which they may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing and surveillance studies. For example, the holder of an approved BLA in the United States is obligated to monitor and report adverse events and any failure of a product to meet the specifications in the BLA. FDA guidance advises that patients treated with some types of gene therapy undergo follow-up observations for potential adverse events for as long as 15 years. Similarly, in the EU, pharmacovigilance obligations are applicable to all medicinal products. In addition to those, holders of a marketing authorization for gene or cell therapy products must detail, in their application, the measures they envisage to ensure follow-up of the efficacy and safety of these products. In cases of particular concern, marketing authorization holders for gene or cell therapy products in the EU may be required to design a risk management system with a view to identifying, preventing or minimizing risks and may be obliged to carry out post-marketing studies. In the United States, the holder of an approved BLA must also submit new or supplemental applications and obtain FDA approval for certain changes to the approved product, product labeling or manufacturing process. Similar provisions apply in the EU. Advertising and promotional materials must comply with FDA rules and are subject to FDA review, in addition to other potentially applicable federal and state laws. Similarly, in the EU any promotion of medicinal products is highly regulated and, depending on the specific jurisdiction involved, may require prior vetting by the competent national regulatory authority.

In addition, product manufacturers and their facilities are subject to payment of user fees and continual review and periodic inspections by the FDA and other regulatory authorities for compliance with cGMP requirements and adherence to commitments made in the BLA or foreign marketing application. If we, our collaborators or a regulatory agency discovers previously unknown problems with a product such as adverse events of unanticipated severity or frequency or problems with the facility where the product is manufactured or disagrees with the promotion, marketing or labeling of that product, a regulatory agency may impose restrictions relative to that product, the manufacturing facility or us or our collaborators, including requiring recall or withdrawal of the product from the market or suspension of manufacturing.

Moreover, if any of our product candidates are approved, our product labeling, advertising, promotion and distribution will be subject to regulatory requirements and continuing regulatory review. The FDA strictly regulates the promotional claims that may be made about drug products. In particular, a product may not be promoted for uses that are not approved by the FDA as reflected in the product's approved labeling.

If we or our collaborators fail to comply with applicable regulatory requirements following approval of any potential products we may develop, authorities may:

- issue an untitled enforcement letter or a warning letter asserting a violation of the law;
- seek an injunction, impose civil and criminal penalties, and impose monetary fines, restitution or disgorgement of profits or revenues;
- suspend or withdraw regulatory approval;

- suspend or terminate any ongoing clinical trials or implement requirements to conduct post-marketing studies or clinical trials;
- refuse to approve a pending BLA or comparable foreign marketing application (or any supplements thereto) submitted by us or our collaborators;
- restrict the labeling, marketing, distribution, use or manufacturing of products;
- seize or detain products or otherwise require the withdrawal or recall of products from the market;
- refuse to approve pending applications or supplements to approved applications that we or our collaborators submit;
- refuse to permit the import or export of products; or
- refuse to allow us or our collaborators to enter into government contracts.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. The occurrence of any event or penalty described above may inhibit our or our collaborators' ability to commercialize products and our ability to generate revenues.

In addition, the FDA's policies, and policies of foreign regulatory agencies, may change, and additional regulations may be enacted that could prevent, limit or delay regulatory approval of product candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the United States or abroad. For example, the results of the 2020 Presidential election and recent change in administration may impact our business and industry. The Trump administration, for example, took several executive actions, including the issuance of a number of Executive Orders, that could impose significant burdens on, or otherwise materially delay, the FDA's ability to engage in routine oversight activities such as implementing statutes through rulemaking, issuance of guidance and review and approval of marketing applications. It is difficult to predict whether or how these requirements will be implemented or whether they will be rescinded or replaced under the Biden Administration. The policies and priorities of the Biden administration are unknown and could materially impact the regulation governing our products. If we or our collaborators are slow or unable to adapt to changes in existing requirements or the adoption of new requirements, or if we or our collaborators are unable to maintain regulatory compliance, marketing approval that has been obtained may be lost and we may not achieve or sustain profitability.

Even if any product we develop alone or with collaborators receives marketing approval, such product 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 any potential therapeutic products we develop alone or with collaborators will depend upon their degree of market acceptance by physicians, patients, third-party payors and others in the medical community. Even if any potential therapeutic products we develop alone or with collaborators receive marketing approval, they 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 any product we develop alone or with collaborators, if approved for commercial sale, will depend on a number of factors, including:

- the efficacy and safety of such product as demonstrated in clinical trials;
- the prevalence and severity of any side effects;
- the clinical indications for which the product is approved by FDA, the EMA or other regulatory authorities;
- product labeling or product insert requirements of the FDA, the EMA or other regulatory authorities, including any limitations or warnings contained in a product's approved labeling;
- public attitudes regarding genome editing technologies;
- our and any collaborators' ability to educate the medical community about the safety and effectiveness of the product;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies, as well as their willingness to accept a therapeutic intervention that involves the editing of the patient's genome;
- the potential and perceived advantages compared to alternative treatments;
- convenience and ease of administration compared to alternative treatments;
- any restrictions on the use of such product together with other treatments or products;
- market introduction of competitive products;

- publicity concerning such product or competing products and treatments;
- the ability to offer such product for sale at a competitive price;
- the strength of marketing and distribution support; and
- sufficient third-party coverage and adequate reimbursement.

If any products we develop alone or with collaborators do not achieve an adequate level of acceptance, we may not generate significant product revenues, 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 products we develop alone or with collaborators, the commercialization of such products may not be successful if and when they are approved.

We do not have a sales or marketing infrastructure and have no experience in the sale, marketing or distribution of biopharmaceutical or other commercial products. To achieve commercial success for any approved products for which we retain sales and marketing responsibilities, we must either develop a sales and marketing organization or outsource these functions to third parties. In the future, we may choose to build a focused sales, marketing and commercial support infrastructure to sell, or participate in sales activities with our collaborators for, certain product candidates if and when they are approved.

There are risks involved with both establishing our own commercial capabilities and entering into arrangements with third parties to perform these services. For example, restricted or closed distribution channels may make it difficult to distribute products to segments of the patient population, and the lack of complementary medicines to be offered by sales personnel may put us at a competitive disadvantage relative to companies with more extensive product lines.

Recruiting and training a sales force or reimbursement specialists are expensive and time consuming and could delay any product launch. If the commercial launch of a product 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, and our investment would be lost if we cannot retain or reposition our commercialization personnel. Factors that may inhibit our efforts to commercialize products on our own include:

- unforeseen costs and expenses associated with creating an independent commercialization organization;
- our inability to recruit, train, retain and effectively manage adequate numbers of effective sales, marketing, customer service and other support personnel, including for reimbursement or medical affairs;
- the inability of sales personnel to educate adequate numbers of physicians on the benefits of our future medicines; and
- the inability of reimbursement professionals to negotiate arrangements for formulary access, reimbursement and other acceptance by payors.

If we choose to enter into arrangements with third parties to perform sales, marketing, commercial support or distribution services, we may not be successful in entering into such arrangements or may be unable to do so on terms that are favorable to us. Entering into such third-party arrangements may subject us to a variety of risks, including:

- product revenues or profitability to us being lower than if we were to market and sell any products we or our collaborators may develop ourselves;
- our inability to exercise direct control over sales and marketing activities and personnel;
- failure of the third parties to devote necessary resources and attention to, or other inability to, sell and market any products we or our collaborators may develop;
- potential disputes with third parties concerning sales and marketing expenses, calculation of royalties and sales and marketing strategies; and
- unforeseen costs and expenses associated with sales and marketing.

If we do not establish effective commercialization capabilities, either on our own or in collaboration with third parties, we will not be successful in commercializing any of our product candidates that may receive approval.

If the market opportunities for any products we develop alone or with collaborators are smaller than our estimates, or if we are unable to successfully identify enough patients, our revenues may be adversely affected.

We focus some of our research and product development on treatments for rare genetic diseases. Our and our collaborators' projections of both the number of people who have these diseases, as well as the subset of people with these diseases who have the potential to benefit from treatment with product candidates we may develop, are based on estimates. These estimates may prove to be incorrect, and new studies may change the estimated incidence or prevalence of these diseases. The number of patients in the United States, Europe and elsewhere may turn out to be lower than expected, and patients may not be amenable to treatment with products that we may develop alone or with collaborators, or may become increasingly difficult to identify or gain access to, any of which would decrease our ability to realize revenue from any such products for such diseases.

The successful commercialization of potential products will depend in part on the extent to which governmental authorities and health insurers establish coverage, and the adequacy of reimbursement levels and pricing policies, and failure to obtain or maintain coverage and adequate reimbursement for any potential products that may receive approval, could limit marketability of those products and decrease our ability to generate revenue.

The availability of coverage and adequacy of reimbursement by government healthcare programs such as Medicare and Medicaid, private health insurers and other third-party payors is essential for most patients to be able to afford prescription medications such as the potential therapeutic products we develop alone or with collaborators. The ability to achieve acceptable levels of coverage and reimbursement for any potential products that may be approved by governmental authorities will have an effect on our and our collaborators' ability to successfully commercialize such products. Even if products we develop alone or with collaborators obtain coverage by a third-party payor, the resulting reimbursement payment rates may not be adequate or may require co-payments that patients find unacceptably high. If coverage and reimbursement in the United States, the EU or elsewhere is not available for any products we develop alone or with collaborators that may be approved, or any reimbursement that may become available is decreased or eliminated in the future, we and our collaborators may be unable to commercialize such products.

There is significant uncertainty related to the insurance coverage and reimbursement of newly approved drugs and biologics. In the United States, third-party payors, including private and governmental payors, such as the Medicare and Medicaid programs, play an important role in determining the extent to which new drugs and biologics will be covered. In August 2019, the CMS published its decision to cover autologous treatment for cancer with T-cells expressing at least one CAR when administered at healthcare facilities enrolled in the FDA risk evaluation and mitigation strategies and used for an FDA-approved indication or for other uses when the product has been FDA-approved and the use is supported in one or more CMS-approved compendia. The Medicare and Medicaid programs increasingly are used as models in the United States for how private payors and other governmental payors develop their coverage and reimbursement policies for drugs and biologics. Some third-party payors may require pre-approval of coverage for new or innovative devices or drug therapies before they will reimburse healthcare providers who use such therapies. We cannot predict at this time what third-party payors will decide with respect to the coverage and reimbursement for any product that we develop alone or with collaborators.

No uniform policy for coverage and reimbursement for products exists among third-party payors in the United States. Therefore, coverage and reimbursement for products can differ significantly from payor to payor. As a result, the coverage determination process is often a time-consuming and costly process that will require us or our collaborators to provide scientific and clinical support for the use of any potential products that may be approved to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. Furthermore, rules and regulations regarding reimbursement change frequently, in some cases on short notice. Obtaining coverage and adequate reimbursement for products we develop alone or with collaborators may be particularly difficult because of the higher prices often associated with drugs administered under the supervision of a physician. In certain instances, payors may not separately reimburse for the product itself, but only for the treatments or procedures in which such product is used. A decision by a third-party payor not to cover or separately reimburse for products that we develop alone or with collaborators or procedures using such products, could reduce physician utilization of any such products that may receive approval.

Third-party payors are increasingly challenging prices charged for pharmaceutical products and services, and many third-party payors may refuse to provide coverage and reimbursement for particular drugs or biologics when an equivalent generic drug, biosimilar or a less expensive therapy is available. If approved, it is possible that a third-party payor may consider any products that we develop alone or with collaborators as substitutable and only offer to reimburse patients for the less expensive product. Pricing of existing third-party therapeutics may limit the amount we will be able to charge for any products that may receive approval even if we or our collaborators show improved efficacy or improved convenience of administration such products. These payors may deny or revoke the reimbursement status of a given product or establish prices for new or existing marketed products at levels that are too low to enable us to realize an appropriate return on our investment in the product. If reimbursement is not available or is available only at limited levels, we or our collaborators may not be able to successfully commercialize any of the products that we develop, even if approved, and we may not be able to obtain a satisfactory financial return on them. Moreover, increasing efforts by governmental and third-

party payors in the United States and abroad to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for newly approved products and, as a result, they may not cover or provide adequate payment for any products we develop alone or with collaborators that may receive approval. We expect to experience pricing pressures in connection with the sale of any products that may receive approval due to the trend toward managed health care, the increasing influence of health maintenance organizations and additional legislative changes. The downward pressure on healthcare costs in general, particularly prescription drugs and biologics and surgical procedures and other treatments, has become intense. As a result, increasingly high barriers are being erected to the entry of new products.

Outside the United States, international operations are generally subject to extensive governmental price controls and other market regulations, and we believe the increasing emphasis on cost-containment initiatives in Europe and elsewhere have and will continue to put pressure on the pricing and usage of any products we develop alone or with collaborators that may receive approval. In many countries, the prices of medical products are subject to varying price control mechanisms as part of national health systems. Other countries allow companies to fix their own prices for medical products, but monitor and control company profits. Additional international price controls or other changes in pricing regulation could restrict the amount that we or our collaborators are able to charge for products that we develop that may receive approval. Accordingly, in markets outside the United States, the reimbursement for such products may be reduced compared with the United States and may be insufficient to generate commercially reasonable revenue and profits.

Our product candidates for which we intend to seek approval as biologic products may face competition sooner than anticipated.

If we are successful in achieving regulatory approval to commercialize any biologic product candidate we develop alone or with collaborators, it may face competition from biosimilar products. In the United States, our product candidates are regulated by the FDA as biologic products subject to approval under the BLA pathway. The Biologics Price Competition and Innovation Act of 2009, or the BPCIA, created an abbreviated pathway for the approval of biosimilar and interchangeable biologic products following the approval of an original BLA. The abbreviated regulatory pathway establishes legal authority for the FDA to review and approve biosimilar biologics, including the possible designation of a biosimilar as "interchangeable" based on its similarity to an existing brand product. Under the BPCIA, an application for a biosimilar product may not be submitted 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 after the reference product was first licensed by the FDA. During this 12-year period of exclusivity, another company may still market a competing version of the reference product if the FDA approves a full 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 their 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. While it is uncertain when such processes intended to implement BPCIA may be fully adopted by the FDA, any such processes could have a material adverse effect on the future commercial prospects for biological product candidates.

We believe that any of our product candidates that are approved as biological products under a BLA should qualify for the 12-year period of exclusivity. However, there is a risk that this exclusivity could be shortened due to congressional action or otherwise, or that the FDA will not consider such product candidates 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 product, once approved, will be substituted for any one of our or our collaborators' reference products in a way that is similar to traditional generic substitution for non-biologic 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 products that we develop alone or with collaborators that may be approved, such products may become subject to competition from such biosimilars, with the attendant competitive pressure and potential adverse consequences.

Additional Risks Related to the Identification, Development and Commercialization of Our Food and Agricultural Product Candidates

The regulatory landscape that may govern any potential food or agricultural products that we or our collaborators may develop is uncertain and may adversely impact the development and commercialization activities of our food platform.

In the United States, the United States Department of Agriculture, or the USDA, regulates, among other things, the introduction (including the importation, interstate movement or release into the environment) of organisms and products altered or produced through genetic engineering determined to be plant pests or for which there is reason to believe are plant pests. Such organisms and products are considered "regulated articles." However, a petitioner may submit a request for a determination by the USDA of "nonregulated status" for a particular article. A petition for determination of nonregulated status must include detailed information, including relevant experimental data and publications, field trial reports and a description of the genotypic differences between the regulated article and the non-modified recipient organism, among other things. Neither we nor, to our knowledge, our collaborators

have obtained a determination from the USDA that any product candidates are not "regulated articles" under these regulations. We cannot predict whether the USDA, advocacy groups or other third parties will contend that these products are regulated articles. The USDA's regulations also require that companies obtain a permit or file a notification before engaging in the introduction (including the importation, interstate movement or release into the environment such as in field trials) of "regulated articles." Additionally, a change in the way the USDA interprets its regulations, or a change in its regulations, could subject our or our collaborators' products to more burdensome regulations, thereby substantially increasing the time and costs associated with developing product candidates. Complying with the USDA's Part 340 regulations, including permitting requirements, is a costly, time-consuming process and could delay or prevent the commercialization of any potential food or agricultural products we or our collaborators may develop.

Any potential food or agricultural products that we or our collaborators develop may also be subject to extensive FDA food product regulations. Under sections 201(s) and 409 of the Federal Food, Drug, and Cosmetic Act, or the FDCA, any substance that becomes or is reasonably expected to become a component of food is a food additive and is therefore subject to FDA premarket review and approval, unless the substance is generally recognized, among qualified experts, as having been adequately shown to be safe under the conditions of its intended use (generally recognized as safe, or GRAS), or unless the use of the substance is otherwise excluded from the definition of a food additive, and any food that contains an unsafe food additive is considered adulterated under section 402(a)(2)(C) of the FDCA. The FDA may classify some or all of the potential food or agricultural products that we or our collaborators may develop as containing a food additive that is not GRAS or otherwise determine that such products contain significant compositional differences from existing plant products that require further review. Such classification would cause these potential products to require pre-market approval, which could delay the commercialization of these products. In addition, the FDA is currently evaluating its approach to the regulation of gene-edited plants. For example, on January 19, 2017, the FDA issued a notice in the Federal Register requesting public comment on the use of genome editing techniques to produce new plant varieties that are used for human or animal food or foods that are derived from such new plant varieties produced using genome editing. Among other things, the notice asked for data and information in response to questions about the safety of foods from gene-edited plants, such as whether categories of gene-edited plants present food safety risks different from other plants produced through traditional plant breeding. If the FDA enacts new regulations or policies with respect to gene-edited plants, such policies could result in additional compliance costs and delay or even prevent the commercialization of any of our product candidates, which could negatively affect our profitability. Any delay in the regulatory consultation process, or a determination that any potential products we or our collaborators may develop do not meet regulatory requirements by the FDA or other regulators, could cause a delay in, or prevent, the commercialization of our products, which may lead to reduced acceptance by the public and an increase in competitor products that may directly compete with ours, or could otherwise negatively impact our business, prospects and results of operations.

On December 21, 2018, the USDA finalized a rule implementing the National Bioengineered Food Disclosure Standard, with an implementation date of January 1, 2020. Under this rule, the label of a bioengineered, or BE, food must include a disclosure that the food is a BE food or contains a BE ingredient, with certain exceptions. This rule defines BE food as "a food that contains genetic material that was has been modified through in vitro recombinant deoxyribonucleic acid, or DNA, techniques and for which the modification could not otherwise be obtained through conventional breeding or found in nature," except in the case of an incidental additive present in food at an insignificant level and that does not have any technical or functional effect in the food. Under this rule, products developed by our collaborators based on our ARCUS technology may be required to be labeled "BE," in which case consumer perception of these products may be adversely affected.

In the European Economic Area, or EEA (which is comprised of the 27 Member States of the European Union, or EU, plus Norway, Liechtenstein, and Iceland), genetically modified foods, or GM foods, can only be authorized for sale on the market once they have been subject to rigorous safety assessments. The procedures for evaluation and authorization of GM foods are notably governed by Regulation (EC) 1829/2003 on GM food and feed and Directive 2001/18/EC (as amended and transposed into EEA member states' law and regulations) on the release of genetically modified organisms, or GMOs, into the environment. If the GMO is not to be used in food or feed, then an application must be made under Directive 2001/18/EC. If the GMO is to be used in food or feed (but it is not cultivated in the EEA) then a single application for both food and feed purposes under Regulation 1829/2003 should be made. If the GMO is used in feed or food and it is cultivated in the EEA, an application for both cultivation and food/feed purposes needs to be carried out under Regulation (EC) 1829/2003. A different EU regulation, Regulation (EC) 1830/2003, regulates the labeling of products that contain GMOs that are placed on the EEA market. Directive 2001/18/EC was amended by Directive (EU) 2015/412 which gives EEA member states more flexibility to allow, restrict or prohibit cultivating GMOs in their territory, on a range of environmental grounds, even if such crops were previously authorized at EEA level. Under Directive 2015/412, EEA member state restrictions or prohibitions can only cover cultivation, and not the free circulation and import of genetically modified seeds and plant propagation material, and should be in conformity with the internal market rules of the EU Treaties.

Further EU legislation may be applicable to GM foods such as Directive 2009/41/EC on contained use of genetically modified micro-organisms and Regulation (EC) 1946/2003 on transboundary movements of GMOs.

We cannot predict whether or when any governmental authority will change its regulations with respect to any potential food or agricultural products that we develop alone or with collaborators. Advocacy groups have engaged in publicity campaigns and filed lawsuits in various countries against companies and regulatory authorities seeking to halt biotechnology approval activities or influence public opinion against genetically engineered products. In addition, governmental reaction to negative publicity concerning genetically edited agricultural products could result in greater regulation of genetic research and derivative products or regulatory costs that render our or our collaborators' development of potential food or agricultural products cost prohibitive. Our collaborators may use or integrate our products or technology into other products in ways that could subject those collaborators or products to additional regulation.

The overall agricultural industry is susceptible to agricultural price changes, and we may be exposed to risks from changes in commodity prices.

Changes in the prices of agricultural products could result in changes in demand for and prices of food and agricultural products that we or our collaborators may develop. We may be susceptible to these changes as a result of factors beyond our control, such as general economic conditions, seasonal fluctuations, weather conditions, demand, food safety concerns, product recalls and government regulations, subsidies or market export tariffs. If demand for agricultural products that we or our collaborators may develop is negatively impacted, our potential revenues under collaboration agreements for such products may decline, which could adversely affect our results of operations.

The successful commercialization of any food or agricultural products we develop will depend in part on our collaborators' ability to produce high-quality plant, vegetative propagation material and seeds cost-effectively on a large scale and to accurately forecast demand for such potential products, and they may be unable to do so.

The production of commercial-scale quantities of food or agricultural products or seeds for them requires the multiplication of the plants, vegetative propagation material or seeds through a succession of plantings and seed harvests. The cost-effective production of high-quality, high-volume quantities of such products or seeds may depend in part on our collaborators' abilities to scale production processes to produce plants and seeds in sufficient quantity to meet demand. Our collaborators' existing or future plant and seed production techniques may not enable timely meeting of large-scale production goals cost-effectively for any potential food or agricultural products that we and our collaborators may develop. Although we have worked with some of the largest plant biotechnology companies to edit gene targets and develop potential product candidates in a variety of crop plants, no commercial food or agricultural products have ever been developed using our technology.

In addition, because of the length of time it takes to produce commercial quantities of marketable plants and seeds, our collaborators will need to make seed production decisions well in advance of food product sales. The ability to accurately forecast demand can be adversely affected by a number of factors outside of their control, including changes in market conditions, environmental factors, such as pests and diseases, and adverse weather conditions.

The commercial success of any consumer-centric food or agricultural products that we or our collaborators may develop is reliant on the needs of food manufacturers and the recognition of shifting consumer preferences.

The commercial success of any consumer-centric products depends in part on the ability of the food manufacturer to accurately determine the shifting needs and desires of the ultimate consumer. We will not control the marketing, distribution labeling or any other aspects of the sale and commercialization of the manufacturers' food products. Consumer preferences may be a significant driver in the success of food manufacturers in their efforts to sell food and agricultural products, including products that we or our collaborators may develop. While current trends indicate that consumer preferences may be moving towards "healthier" options, we cannot predict whether such trends will continue or which types of food products will be demanded by consumers in the future. Additionally, as health and nutritional science continues to progress, consumer perception of what foods, nutrients and ingredients are considered "healthy" may shift. We and our collaborators may not be dynamic enough in responding to consumer trends and creating products that will be demanded by consumers in the future. In addition, if consumer demand is lower than our estimates or those of our collaborators, our ability to realize revenues from potential food or agricultural products may be limited. Failure by our collaborators to successfully recognize consumer trends could lower demand for potential food or agricultural products that we or our collaborators may develop, which could harm our business, results of operations and financial condition.

Some of the potential food products we develop alone or with collaborators may be distributed into markets or countries in which they have not received regulatory approval, which may result regulatory challenges or lawsuits.

The scale of the agricultural industry may make it difficult to monitor and control the distribution of any potential food products that we develop alone or with collaborators. As a result, such products may be sold inadvertently within jurisdictions where they are not approved for distribution. Such sales may lead to regulatory challenges or lawsuits against us, which could result in significant expenses and divert our management's attention, which could harm our business, results of operations and financial condition.

Risks Related to Our Organization, Structure and Operations

The ongoing novel coronavirus disease, COVID-19 has impacted our business, and any other pandemic, epidemic or outbreak of an infectious disease may materially and adversely impact our business, including our preclinical studies and clinical trials.

In March 2020, the World Health Organization designated the outbreak of the novel strain of coronavirus known as COVID-19 as a global pandemic, and COVID-19 has spread to multiple global regions, including the United States and Europe. The ongoing pandemic and government measures taken in response have also had a significant impact, both direct and indirect, on businesses and commerce, as worker shortages have occurred; supply chains have been disrupted; facilities and production have been suspended; and demand for certain goods and services, such as medical services and supplies, has spiked, while demand for other goods and services, such as travel, has fallen. In response to the spread of COVID-19 and in accordance with local guidelines, we have implemented measures to mitigate exposure risks and support operations. The health and safety program we have initiated requiring mandatory use of face masks, social distancing, sanitary handwashing practices, use of personal protective equipment stations, stringent cleaning and sanitization of all facilities and measures to reduce total occupancy in facilities, as well as temperature and symptom screening procedures at each location may not sufficiently protect our employees. We have communicated to our employees that based on their comfort level, regardless of role, they may elect not to come to work. Any resurgence of outbreaks or new regulatory orders or guidance or self-imposed protective measures we impose could require reversal of our previously eased restrictions to our on-site activities and, as a result, adversely impact our business, including our preclinical studies and clinical trials.

As a result of the COVID-19 pandemic or other pandemic, epidemic or outbreak of an infectious disease, we have and may continue to experience disruptions that could severely impact our business, preclinical studies and clinical trials, 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;
- diversion of healthcare resources away from the conduct of clinical trials, including the diversion of hospitals serving as our clinical trial sites and hospital staff supporting the conduct of our clinical trials;
- interruption of key clinical trial activities, such as clinical trial site data monitoring, due to limitations on travel imposed or recommended by federal or state governments, employers and others or interruption of clinical trial subject visits and study procedures, which may impact the integrity of subject data and clinical study endpoints;
- interruption or delays in the operations of the FDA or other regulatory authorities, which may impact review and approval timelines;
- interruption of, or delays in receiving, supplies of our product candidates from our contract manufacturing organizations due to staffing shortages, production slowdowns or stoppages and disruptions in delivery systems;
- interruptions in preclinical studies due to restricted or limited operations at our laboratory facility;
- limitations on employee resources that would otherwise be focused on the conduct of our preclinical studies and clinical trials, including because of sickness of employees or their families or the desire of employees to avoid contact with large groups of people; and
- interruption or delays to our sourced discovery and clinical activities.

The COVID-19 pandemic continues to rapidly evolve. Disruptions, competing resource demands and safety concerns caused by the COVID-19 pandemic have caused, and may continue to cause, delays in our clinical trial site activation and our ability to enroll patients. We may also experience other difficulties, disruptions or delays in conducting preclinical studies or initiating, enrolling, conducting or completing our planned and ongoing clinical trials, and we may incur other unforeseen costs as a result. The extent to which the outbreak impacts our business, preclinical studies and clinical trials will depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the ultimate geographic spread of the disease, the duration of the pandemic, travel restrictions and social distancing in the United States and other countries, business closures or business disruptions and the effectiveness of actions taken in the United States and other countries to contain and treat the disease. If we or any of the third parties with whom we engage were to experience shutdowns or any further business disruptions, our ability to conduct our business in the manner and on the timelines presently planned could be materially and negatively impacted. Additionally, the magnitude of the economic impact brought by and the duration of the COVID-19 pandemic is difficult to assess or predict and may continue to result in significant disruption of global financial markets, which may reduce our ability to access capital and negatively affect our liquidity.

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, 2020, we had 231 full-time employees. We will need to significantly expand our organization, and our future financial performance, ability to develop and commercialize product candidates alone or with collaborators and ability to compete effectively will depend in part on our ability to effectively manage any future growth. We may have difficulty identifying, hiring and integrating new personnel. Many of the biotechnology companies that we compete against for qualified personnel and consultants have greater financial and other resources, different risk profiles and a longer history than we do. If we are unable to continue to attract and retain high-quality personnel and consultants, the rate and success at which we can identify and develop product candidates, enter into collaborative arrangements and otherwise operate our business will be limited.

Future growth would impose significant additional responsibilities on our management, including the need to identify, recruit, maintain, motivate and integrate additional employees, consultants and contractors.

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 to managing these growth activities. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expected expansion of our operations or recruit and train additional qualified personnel. Moreover, the expected physical expansion of our operations may lead to significant costs and may divert our management and business development resources from other projects, such as the development of product candidates. If we are not able to effectively manage the expansion of our operations, it may result in weaknesses in our infrastructure, increase our expenses more than expected, give rise to operational mistakes, loss of business opportunities, loss of employees and reduced productivity. Our future financial performance, ability to successfully commercialize any of our product candidates and our ability to compete effectively will depend, in part, on our ability to effectively manage any future growth.

We may engage in transactions that could disrupt our business, cause dilution to our stockholders or reduce our financial resources.

In the future, we may enter into transactions to acquire or in-license rights to product candidates, products or technologies or to acquire other businesses. If we do identify suitable candidates, we may not be able to enter into such transactions on favorable terms, or at all. Any such acquisitions or in-licenses may not strengthen our competitive position, and these transactions may be viewed negatively by customers or investors. We may decide to incur debt in connection with an acquisition or in-license, which may negatively impact our financial condition and restrict our operations, or issue our common stock or other equity securities to the stockholders of the acquired company, which would reduce the percentage ownership of our existing stockholders. We could incur losses resulting from undiscovered liabilities of the acquired business that are not covered by the indemnification we may obtain from the sellers of the acquired business. In addition, we may not be able to successfully integrate the acquired personnel, technologies and operations into our existing business in an effective, timely and non-disruptive manner. Such transactions may also divert management attention from day-to-day responsibilities, increase our expenses and reduce our cash available for operations and other uses. We cannot predict the number, timing or size of future acquisitions or in-licenses or the effect that they might have on our operating results.

Our future success depends on our ability to retain our key executives and to attract, retain and motivate qualified personnel.

We are highly dependent on the research and development experience, technical skills, leadership and continued service of certain members of our management and scientific teams. Although we have formal employment agreements with our executive officers, these agreements do not prevent them from terminating their employment with us at any time upon thirty days' written notice. The loss of the services of any of these persons could impede the achievement of our research, development and commercialization objectives.

Recruiting and retaining qualified scientific, clinical, manufacturing and, if we retain commercialization responsibility for any product candidate we develop alone or with collaborators, sales and marketing personnel will also be critical to our success. We may not be able to attract and retain these personnel on acceptable terms or at all given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. 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 strategies. 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. The inability to recruit, integrate, motivate and retain additional skilled and qualified personnel, or the loss of services of certain executives, key employees, consultants or advisors, may impede the progress of our research, development and commercialization objectives and have a material adverse effect on our business.

We are subject to increased costs as a result of operating as a public company, and our management will be required to devote substantial time to maintaining compliance initiatives and corporate governance practices, including establishing and maintaining proper and effective internal control over financial reporting.

As a public company, we have incurred and will continue to incur significant legal, accounting and other expenses that we did not incur as a private company. We are subject to the Securities Exchange Act of 1934, as amended, or the Exchange Act, including the reporting requirements thereunder, the Sarbanes-Oxley Act of 2002, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of The Nasdaq Stock Market LLC, or Nasdaq, and other applicable securities rules and regulations, including requirements related to the establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel will need to continue to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations have increased our legal and financial compliance costs, making some activities more difficult, time consuming or costly, and increasing demand on our systems and resources.

Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404, we are required to furnish a report by our management on our internal control over financial reporting. However, while we remain an emerging growth company, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404 of the Sarbanes-Oxley Act within the prescribed period, we will be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. We may need to hire more employees in the future or engage outside consultants to comply with these requirements, which will further increase our costs and expenses. If we fail to implement the requirements of Section 404 of the Sarbanes-Oxley Act in the required timeframe, we may be subject to sanctions or investigations by regulatory authorities, including the SEC and Nasdaq. Furthermore, if we are unable to conclude that our internal control over financial reporting is effective, our investors may lose confidence in the accuracy and completeness of our financial reports, the market price of our common stock could decline, and we could be subject to sanctions or investigations by regulatory authorities. Failure to implement or maintain an effective internal control system could also restrict our future access to the capital markets.

Our business and operations would suffer in the event of system failures or security breaches.

Despite the implementation of security measures, our computer systems, as well as those of third parties with which we have relationships, are vulnerable to damage from computer viruses, unauthorized access, natural and manmade disasters, terrorism, war and telecommunication and electrical failures. Attacks upon information technology systems are increasing in their frequency, levels of persistence, sophistication and intensity, and are being conducted by sophisticated and organized groups and individuals with a wide range of motives and expertise. As a result of the COVID-19 pandemic, we may also face increased cybersecurity risks due to our reliance on internet technology and the number of our employees who are working remotely, which may create additional opportunities for cybercriminals to exploit vulnerabilities. Furthermore, because the technologies used to obtain unauthorized access to, or to sabotage, systems change frequently and often are not recognized until launched against a target, we may be unable to anticipate these techniques or implement adequate preventative measures. We may also experience security breaches that may remain undetected for an extended period. While we do not believe that we have experienced any such system failure, accident or security breach to date, if such an event were to occur and cause interruptions in our or their operations, it could result in delays and/or material disruptions of our research and development programs. For example, the loss of trial data from completed, ongoing or planned trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of or damage to data or applications, or inappropriate disclosure of personal, confidential or proprietary information, we could incur liability and the development of our product candidates could be delayed.

The U.S. federal and various state and foreign governments have enacted or proposed requirements regarding the collection, distribution, use, security and storage of personally identifiable information and other data relating to individuals, and U.S. federal and state consumer protection laws are being applied to enforce regulations related to the online collection, use and dissemination of data. In the ordinary course of our business, we and third parties with which we have relationships will continue to collect and store sensitive data, including intellectual property, clinical trial data, proprietary business information, personal data and personally identifiable information of our clinical trial subjects and employees, in data centers and on networks. The secure processing, maintenance and transmission of this information is critical to our operations. Despite our and our collaborators' security measures, our information technology and infrastructure may be vulnerable to attacks by hackers or internal bad actors, breaches due to employee error, technical vulnerabilities, malfeasance or other disruptions. A number of proposed and enacted federal, state and international laws and regulations obligate companies to notify individuals of security breaches involving particular personally identifiable information, which could result from breaches experienced by us or by third parties, including collaborators, vendors, contractors or other organizations with which we have formed strategic relationships. Although, to our knowledge, neither we nor any such third parties have experienced any material security breach, and even though we may have contractual protections with such third parties, any such breach could compromise our or their networks and the information stored there could be accessed, publicly disclosed, lost or stolen. Any such access, disclosure, notifications, follow-up actions related to such a security breach or other loss of

information could result in legal claims or proceedings, liability under laws that protect the privacy of personal information and significant costs, including regulatory penalties, fines and legal expenses, and such an event could disrupt our operations, cause us to incur remediation costs, damage our reputation and cause a loss of confidence in us and our or such third parties' ability to conduct clinical trials, which could adversely affect our reputation and delay our research and development programs.

Our insurance policies are expensive and protect us only from some business risks, which leaves us exposed to significant uninsured liabilities.

We do not carry insurance for all categories of risk that our business may encounter. If we obtain marketing approval for any product candidates that we or our collaborators may develop, we intend to acquire insurance coverage to include the sale of commercial products, but we may be unable to obtain such insurance on commercially reasonable terms or in adequate amounts. We do not carry specific biological or hazardous waste insurance coverage, and our property, casualty and general liability insurance policies specifically exclude coverage for damages and fines arising from biological or hazardous waste exposure or contamination.

Accordingly, in the event of contamination or injury, we could be held liable for damages or be penalized with fines in an amount exceeding our resources, and clinical trials or regulatory approvals for any of our product candidates could be suspended. We also expect that operating as a public company will make it more expensive for us to obtain director and officer liability insurance, and we may be required to accept reduced policy limits and coverage or incur substantially higher costs to obtain the same or similar coverage. As a result, it may be more difficult for us to attract and retain qualified individuals to serve on our board of directors, our board committees or as our executive officers.

Insurance coverage is becoming increasingly expensive, and in the future we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses. We do not know if we will be able to maintain existing insurance with adequate levels of coverage, and any liability insurance coverage we acquire in the future may not be sufficient to reimburse us for any expenses or losses we may suffer. A successful liability claim or series of claims brought against us could require us to pay substantial amounts and cause our share price to decline and, if judgments exceed our insurance coverage, could adversely affect our results of operations and business, including preventing or limiting the development and commercialization of any product candidates that we or our collaborators may develop.

If we or any of our contract manufacturers or other suppliers fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur significant costs.

We and any of our contract manufacturers and suppliers are subject to numerous federal, state and local environmental, health and safety laws, regulations and permitting requirements, including those governing laboratory procedures; the generation, handling, use, storage, treatment and disposal of hazardous and regulated materials and wastes; the emission and discharge of hazardous materials into the ground, air and water; and employee health and safety. Our operations involve the use of hazardous and flammable materials, including chemicals and biological and radioactive materials. Our operations also produce hazardous waste. 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. Under certain environmental laws, we could be held responsible for costs relating to any contamination at our current or past facilities and at third-party facilities. We also could incur significant costs associated with civil or criminal fines and penalties.

Compliance with applicable environmental laws and regulations may be expensive, and current or future environmental laws and regulations may impair our research and product development efforts. In addition, we cannot entirely eliminate the risk of accidental injury or contamination from these materials or wastes.

Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not carry specific biological or hazardous waste insurance coverage, and our property, casualty and general liability insurance policies (under which we currently have an aggregate of approximately $10 million in coverage) specifically exclude coverage for damages and fines arising from biological or hazardous waste exposure or contamination. Accordingly, in the event of contamination or injury, we could be held liable for damages or be penalized with fines in an amount exceeding our resources, and our clinical trials or regulatory approvals for any product candidate we develop alone or with collaborators could be suspended, which could have a material adverse effect on our business and financial condition.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws, regulations and permitting requirements, and any third-party contract manufacturers and suppliers we engage will also be subject to such current and future regulations and requirements. These current or future laws, regulations and permitting requirements may impair our research, development or production efforts. Failure to comply with these laws, regulations and permitting requirements, either by us

or by any third-party contract manufacturers and suppliers we engage, also may result in substantial fines, penalties or other sanctions or business disruption.

Our business operations, including our current and future relationships with third parties, will expose us to penalties for potential misconduct or improper activity, including non-compliance with regulatory standards and requirements.

Complex laws constrain our business and the financial arrangements and relationships through which we conduct our operations, including how we may research, market, sell and distribute product candidates alone or with collaborators. We are exposed to the risk of fraud or other misconduct by our employees, consultants and collaborators and, if we or our collaborators commence clinical trials and proceed to commercialization, our principal investigators and commercial partners, as well as healthcare professionals, third-party payors, patient organizations and customers. For example, misconduct by these parties could include intentional failures to comply with FDA regulations or the regulations applicable in the EU and other jurisdictions, provide accurate information to the FDA, the European Commission and other regulatory authorities, comply with healthcare fraud and abuse laws and regulations in the United States and abroad, report financial information or data accurately or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, false and/or misleading statements, corruption of government officials, self-dealing and other abusive practices. These laws and regulations restrict or prohibit a wide range of pricing, discounting, marketing, promotion, sales commission and customer incentive programs and other business arrangements. Such misconduct also could involve the improper use or misrepresentation of information obtained in the course of clinical trials, creating fraudulent data in preclinical studies or clinical trials, illegal misappropriation of study materials or other property, or improper interactions with the FDA or other regulatory authorities, which could result in regulatory sanctions and cause serious harm to our or our collaborators' reputations.

Ensuring that our internal operations and current and future business arrangements with third parties comply with applicable healthcare laws and regulations will involve substantial costs. Additionally, we are subject to the risk that a person or government could allege such fraud or other misconduct, even if none occurred. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations, agency guidance 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 the laws described above or any other governmental laws and regulations that may apply to us, we may be subject to significant penalties, including civil, criminal and administrative penalties, damages, fines, exclusion from government-funded healthcare programs, such as Medicare and Medicaid or similar programs in other countries or jurisdictions, additional reporting requirements and oversight if subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, disgorgement, individual imprisonment, contractual damages, reputational harm, diminished profits and the curtailment or restructuring of our operations. If any of the physicians or other providers or entities with whom we expect to do business are found to not be in compliance with applicable laws, they may be subject to similar penalties, such as criminal, civil or administrative sanctions, including exclusions from government-funded healthcare programs and imprisonment, which could affect our ability to operate our business. Further, defending against any such actions can be costly and time-consuming and may require significant 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.

We have adopted policies applicable to all of our employees, but it is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent such activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from government investigations or other actions or lawsuits stemming from a failure to comply with applicable laws or regulations. Additionally, we are subject to the risk that a person could allege such fraud or other misconduct, even if none occurred. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could result in the imposition of any of the penalties discussed above and have a significant impact on our business and financial condition.

We are subject to complex tax rules relating to our business, and any audits, investigations or tax proceedings could have a material adverse effect on our business, results of operations and financial condition.

We are subject to income and non-income taxes in the United States. Income tax accounting often involves complex issues, and judgment is required in determining our provision for income taxes and other tax liabilities. In May 2018 we formed a subsidiary in Australia, in June 2019 we formed a subsidiary in the United Kingdom, and we may operate in other non-US jurisdictions in the future. We could become subject to income and non-income taxes in non-US jurisdictions as well. In addition, many jurisdictions have detailed transfer pricing rules, which require that all transactions with non-resident related parties be priced using arm's length pricing principles within the meaning of such rules. The application of withholding tax, goods and services tax, sales taxes and other non-income taxes is not always clear and we may be subject to tax audits relating to such withholding or non-income taxes. We believe that our tax positions are reasonable and our tax reserves are adequate to cover any potential liability. We are currently not subject to any tax audits. However, the Internal Revenue Service or other taxing authorities may disagree with our positions. If the Internal Revenue Service or any other tax authorities were successful in challenging our positions, we may be liable for additional tax and

penalties and interest related thereto or other taxes, as applicable, in excess of any reserves established therefor, which may have a significant impact on our results and operations and future cash flow.

We may not be able to utilize all, or any, of our net operating loss carryforwards.

We have incurred substantial losses during our history, do not expect to become profitable in the near future, and we may never achieve profitability. As of December 31, 2020, we had U.S. federal, state, and foreign net operating loss carryforwards of $172.7 million, $116.5 million, and $0.6 million, respectively. Our federal net operating loss carryforwards of $19.7 million will begin to expire in 2030 while the remaining federal net operating loss carryforwards of $153.0 million carry forward indefinitely. The state net operating loss carryforwards begin to expire in 2025. In addition, as of December 31, 2020, we have U.S. federal and state research and development tax credits of $9.9 million and an amount less than $0.1 million available to offset future U.S. federal and state income taxes, which begin to expire in 2027 and 2030, respectively. At December 31, 2020 and December 31, 2019, we had federal Orphan Drug credits of $6.0 million and $1.8 million, respectively, which begin to expire in 2038.

Changes in tax laws or regulations may adversely impact our ability to utilize all, or any, of our net operating loss carryforwards. For example, legislation enacted in 2017, informally titled the Tax Cuts and Jobs Act, significantly revised the Internal Revenue Code of 1986, as amended. Future guidance from the Internal Revenue Service and other tax authorities with respect to the Tax Cuts and Jobs Act may affect us, and certain aspects of the Tax Cuts and Jobs Act could be repealed or modified in future legislation. For example, the CARES Act modified certain provisions of the Tax Cuts and Jobs Act. Under the CARES Act, net operating losses arising in a tax year beginning after December 31, 2017, and before January 1, 2021, generally may now be carried back five years. Under the Tax Cuts and Jobs Act, as modified by the CARES Act, unused losses generated in taxable years ending after December 31, 2017 will not expire and may be carried forward indefinitely, but the deductibility of such net operating losses in tax years beginning after December 31, 2020, is limited to 80% of taxable income. It is uncertain if and to what extent various states will conform to the to the Tax Cuts and Jobs Act or the CARES Act.

As of December 31, 2020, we have a valuation allowance for the full amount of our net deferred tax assets as the realization of the net deferred tax assets is not determined to be more likely than not. In addition, Sections 382 and 383 of the Code limit a corporation's ability to utilize its net operating loss carryforwards and certain other tax attributes (including research credits) to offset any future taxable income or tax if the corporation experiences a cumulative ownership change of more than 50% over any rolling three-year period. State net operating loss carryforwards (and certain other tax attributes) may be similarly limited. A Section 382 ownership change can therefore result in significantly greater tax liabilities than a corporation would incur in the absence of such a change, and any increased liabilities could adversely affect the corporation's business, results of operations, financial condition and cash flow. We have not yet determined if any prior change in the ownership of our equity or any change in such ownership in connection with our IPO, would trigger a Section 382 ownership change. It is possible that such a Section 382 ownership change has already occurred in prior periods. Furthermore, additional ownership changes may occur in the future as a result of events over which we will have little or no control, including purchases and sales of our equity by our 5% stockholders, the emergence of new 5% stockholders, additional equity offerings or redemptions of our stock or certain changes in the ownership of any of our 5% stockholders. As a result, our pre-2018 net operating loss carryforwards (and research tax credits) may expire prior to being used, and our net operating loss carryforwards and tax credits generated in 2018 and thereafter will be subject to a percentage limitation, upon an ownership change. Similar provisions of state tax law may also apply to limit our use of accumulated state tax attributes. As a result, even if we attain profitability, we may be unable to use all or a material portion of our NOLs and other tax attributes, which could adversely affect our future cash flows.

Risks Related to Our Reliance on Third Parties

We have entered into significant arrangements with collaborators and expect to depend on collaborations with third parties for certain research, development and commercialization activities, and if any such collaborations are not successful, it may harm our business and prospects.

We have sought in the past, and anticipate that we will continue to seek in the future, third-party collaborators for the research, development and commercialization of certain product candidates and the research and development of certain technologies. For example, we are party to the Servier Agreement and the Development and License Agreement with Lilly. Under these agreements, we are focused on research and development of allogeneic CAR T cell therapies that utilize or incorporate our genome editing technologies and in vivo gene editing products that utilize or incorporate our ARCUS nucleases. In addition, our food platform is based on a consumer-centric model, whereby our research and development activities and potential revenues are based on the needs and commercial success of our collaborators. Our likely collaborators for other product research and development arrangements include large and mid-size pharmaceutical and biotechnology companies biotechnology and food, beverage, nutrition and agricultural biotechnology companies, and our likely collaborators for other technology research and development arrangements include universities and other research institutions.

Working with collaborators poses several significant risks. We have limited control over the amount and timing of resources that our collaborators dedicate to the product candidates or technologies we may seek to develop with them. A variety of factors may impact resource allocation decisions of collaborators, such as study or trial results, changes in the collaborator's strategic focus, turnover in personnel responsible for the development activities, financial capacity or external factors such as a business combination or change in control that diverts resources or creates competing priorities. Collaboration agreements may not lead to development or commercialization of product candidates or the development of technologies in the most efficient manner or at all. Resource allocation and other developmental decisions made by our collaborators may result in the delay or termination of research programs, studies or trials, repetition of or initiation of new studies or trials or provision of insufficient funding or resources for the completion of studies or trials or the successful marketing and distribution of any product candidates that may receive approval. Collaborators could independently develop, or develop with third parties, product candidates or technologies that compete directly or indirectly with our product candidates or technologies if the collaborators believe that competitive products or technologies are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours. Collaborators may not properly obtain, maintain, enforce or defend our intellectual property or proprietary rights or may use our proprietary information in such a way that could jeopardize or invalidate our proprietary information or expose us to potential litigation. Disputes may arise between us and our collaborators that result in the delay or termination of the research, development or commercialization activities or that result in costly litigation or arbitration that diverts management attention and resources.

Our ability to generate revenues from these arrangements will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements. If our collaborations do not result in the successful development and commercialization of product candidates or technologies, or if one of our collaborators terminates its agreement with us, we may not receive any future funding or milestone or royalty payments under the collaboration. If we do not receive the funding we expect under these agreements, our development of product candidates or technologies could be delayed, and we may need additional resources to develop such product candidates or technologies. For example, as a result of the termination of the Gilead Agreement, we are no longer entitled to receive certain milestone payments, our submission of an IND for our in vivo chronic HBV program has been delayed and we are currently exploring alternative opportunities to enable to continued development of ARCUS-based HBV therapies. In connection with this termination, and if any of our other collaborators terminates its agreement with us, we may be unable to find a suitable replacement collaborator or any replacement collaborator or attract new collaborators and may need to raise additional capital to pursue further development or commercialization of the applicable product candidates or technologies. These events could delay development programs, negatively impact the perception of our company in business and financial communities or cause us to have to cease development of the product candidate covered by the collaboration arrangement. Failure to develop or maintain relationships with any current collaborators could result in the loss of opportunity to work with that collaborator or reputational damage that could impact our relationships with other collaborators in the relatively small industry communities in which we operate. Moreover, all of the risks relating to product development, regulatory approval and commercialization described in this Annual Report on Form 10-K apply to the activities of our collaborators. If our existing collaboration agreements or any collaborative or strategic relationships we may establish in the future are not effective and successful, it may damage our reputation and business prospects, delay or prevent the development and commercialization of product candidates and inhibit or preclude our ability to realize any revenues.

If we are not able to establish collaborations on commercially reasonable terms, we may have to alter our research, development and commercialization plans.

Our research and product development programs and the potential commercialization of any product candidates we develop alone or with collaborators will require substantial additional cash to fund expenses, and we expect that we will continue to seek collaborative arrangements with others in connection with the development and potential commercialization of current and future product candidates or the development of ancillary technologies. We face significant competition in establishing relationships with appropriate collaborators. 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. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Those factors may include, among other things and as applicable for the type of potential product or technology, an assessment of the opportunities and risks of our technology, the design or results of studies or trials, the likelihood of approval, if necessary, by the USDA, the FDA or similar regulatory authorities outside the United States, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing products and technologies and industry and market conditions generally.

Current or future 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. Additionally, we may be restricted under existing collaboration agreements from entering into future agreements on certain terms or for certain development activities with potential collaborators. For example, we have granted exclusive rights or options to Servier for certain targets, and during the terms of our respective collaboration agreements with them we will be restricted from granting rights to other parties to use our ARCUS technology to pursue potential products that address those targets. Similarly, our collaboration agreements have in the

past and may in the future contain non-competition provisions that could limit our ability to enter into strategic collaborations with future collaborators.

Collaborations are complex and time-consuming to negotiate and document. We may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. If we do enter into additional collaboration agreements, the negotiated terms may force us to relinquish rights that diminish our potential profitability from development and commercialization of the subject product candidates or others. If we are unable to enter into additional collaboration agreements, we may have to curtail the research and development of the product candidate or technology for which we are seeking to collaborate, reduce or delay research and development programs, delay potential commercialization timelines, reduce the scope of any sales or marketing activities or undertake research, development or commercialization activities at our own expense. If we elect to increase our expenditures to fund research, development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all.

We expect to rely on third parties to conduct, supervise and monitor our clinical trials and some aspects of our research and preclinical testing, and if those third parties do not successfully carry out their contractual duties, comply with regulatory requirements, or otherwise perform in a satisfactory manner, we may not be able to obtain regulatory approval or commercialize product candidates, or such approval or commercialization may be delayed, and our business may be substantially harmed.

We may rely on medical institutions, universities, clinical investigators, contract laboratories and other third parties, such as CROs, to conduct preclinical studies and future clinical trials for our product candidates. Nevertheless, we will be responsible for ensuring that each of our studies and trials is conducted in accordance with the applicable protocol, legal and regulatory requirements and scientific standards, and our reliance on such third parties will not relieve us of our regulatory responsibilities.

Although we intend to design the trials for our product candidates either alone or with collaborators, third parties may conduct all of the trials. As a result, many important aspects of our research and development programs, including their conduct and timing, will be outside of our direct control. Our reliance on third parties to conduct future studies and trials will also result in less direct control over the management of data developed through studies and trials than would be the case if we were relying entirely upon our own staff. Communicating with outside parties can also be challenging, potentially leading to mistakes and difficulties in coordinating activities. Outside parties may have staffing difficulties, fail to comply with contractual obligations, experience regulatory compliance issues, undergo changes in priorities, become financially distressed or form relationships with other entities, some of which may be our competitors. We also face the risk of potential unauthorized disclosure or misappropriation of our intellectual property by CROs or other third parties, which may reduce our trade secret protection and allow our potential competitors to access and exploit our proprietary technology. For any violations of laws and regulations during the conduct of our preclinical studies and future clinical trials, we could be subject to warning letters or enforcement action that may include civil penalties up to and including criminal prosecution.

For example, we will remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA requires us to comply with regulations, commonly referred to as Good Clinical Practices, or GCPs, for conducting, monitoring, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. If we, our collaborators, our CROs or other third parties fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable and FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We also are required to register certain ongoing clinical trials and post the results of such completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within certain timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

If our CROs or other third parties do not successfully carry out their contractual duties or obligations, fail to meet expected deadlines, or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols or regulatory requirements or for any other reasons, trials for product candidates may be extended, delayed or terminated, and we or our collaborators may not be able to obtain regulatory approval for, or successfully commercialize, any product candidate that we develop. If we are required to repeat, extend the duration of or increase the size of any trials we conduct, it could significantly delay commercialization and require significantly greater expenditures. As a result of any of these factors, our financial results and the commercial prospects for any product candidate that we or our collaborators may develop would be harmed, our costs could increase and our ability to generate revenues could be delayed.

We expect to rely on third parties to supply raw materials or manufacture product supplies that are necessary for the conduct of preclinical studies, clinical trials and manufacturing of our product candidates, and failure by third parties to provide us with sufficient quantities of products, or to do so at acceptable quality levels or prices and on a timely basis, could harm our business.

We are dependent on third parties for the supply of various biological materials, such as cells, cytokines and antibodies, and the manufacture of product supplies, such as media, plasmids, mRNA and AAV viral vectors, that are necessary to produce our product candidates. The supply of these materials could be reduced or interrupted at any time. In such case, identifying and engaging an alternative supplier or manufacturer could result in delay, and we may not be able to find other acceptable suppliers or manufacturers on acceptable terms, or at all. Switching suppliers or manufacturers may involve substantial costs and is likely to result in a delay in our desired clinical and commercial timelines. If we change suppliers or manufacturers for commercial production, applicable regulatory agencies may require us to conduct additional studies or trials. If key suppliers or manufacturers are lost, or if the supply of the materials is diminished or discontinued, we or our collaborators may not be able to develop, manufacture and market product candidates in a timely and competitive manner, or at all. If any of our product candidates receives approval, we will likely need to seek alternative sources of supply of raw materials or manufactured product supplies and there can be no assurance that we will be able to establish such relationships to provide such supplies on commercially reasonable terms or at acceptable quality levels, if at all. If we are unable to identify and procure additional sources of supply that fit our required needs, we could face substantial delays or incur additional costs in procuring such materials. In addition, manufactured product supplies are subject to stringent manufacturing processes and rigorous testing. Delays in the completion and validation of facilities and manufacturing processes of these materials could adversely affect the ability to complete studies or trials and commercialize any product candidates that may receive approval. Furthermore, if our suppliers or manufacturers encounter challenges relating to employee turnover, the supply and manufacturing of our materials could be delayed or adversely affected as such parties seek to hire and train new employees. These factors could cause the delay of studies or trials, regulatory submissions, required approvals or commercialization of product candidates that we or our collaborators may develop, cause us to incur higher costs and prevent us from commercializing products successfully. Furthermore, if our suppliers or manufacturers fail to meet contractual requirements, and we are unable to secure one or more replacements capable of production at a substantially equivalent cost, our or our collaborators' studies or trials may be delayed and we could lose potential revenue.

We may rely on third parties for at least a portion of the manufacturing process of product candidates, and failure by those parties to adequately perform their obligations could harm our business.

While we expect to use our MCAT facility for certain of our clinical-scale manufacturing and processing needs, we may continue to rely on outside vendors for at least a portion of the manufacturing process of product candidates that we or our collaborators may develop. The facilities used by our contract manufacturers to manufacture product candidates must be approved by the FDA or other foreign regulatory agencies pursuant to inspections that will be conducted after we submit an application to the FDA or other foreign regulatory agencies. To the extent that we or our collaborators engage third parties for manufacturing services, we will not control the manufacturing process of, and will be completely dependent on, our contract manufacturing providers for compliance with cGMP requirements for manufacture of the product candidates. We have not yet caused any product candidates to be manufactured or processed on a commercial scale and may not be able to do so. We will make changes as we work to optimize the manufacturing process, and we cannot be sure that even minor changes in the process will result in products that are safe and effective. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or other regulatory authorities, they will not be able to secure and/or maintain regulatory approval for their 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 authority does not approve these facilities for the manufacture of product candidates or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market any of our or our collaborators' potential products.

Risks Related to Intellectual Property

Our ability to compete may decline if we do not adequately protect our proprietary rights, and if our proprietary rights do not provide a competitive advantage.

Our commercial success depends upon obtaining and maintaining proprietary rights to our intellectual property estate, including rights relating to ARCUS and to our product candidates, as well as successfully defending these rights against third-party challenges and successfully enforcing these rights to prevent third-party infringement. We will only be able to protect ARCUS and product candidates from unauthorized use by third parties to the extent that valid and enforceable patents cover them. Our ability to obtain and maintain patent protection for ARCUS and our product candidates is uncertain due to a number of factors, including that:

- we may not have been the first to invent the technology covered by our pending patent applications or issued patents;

- we may not be the first to file patent applications covering product candidates, including their compositions or methods of use, as patent applications in the United States and most other countries are confidential for a period of time after filing;
- our compositions and methods may not be patentable;
- our disclosures in patent applications may not be sufficient to meet the statutory requirements for patentability;
- any or all of our pending patent applications may not result in issued patents;
- others may independently develop identical, similar or alternative technologies, products or compositions or methods of use thereof;
- others may design around our patent claims to produce competitive technologies or products that fall outside of the scope of our patents;
- we may fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection;
- we may not seek or obtain patent protection in countries that may eventually provide us a significant business opportunity;
- any patents issued to us may not provide a basis for commercially viable products, may not provide any competitive advantages or may be successfully challenged by third parties;
- others may identify prior art or other bases upon which to challenge and ultimately invalidate our patents or otherwise render them unenforceable; and
- the growing scientific and patent literature relating to engineered endonucleases, including our own patents and publications, may make it increasingly difficult or impossible to patent new engineered nucleases in the future.

Even if we have or obtain patents covering ARCUS or any product candidates or compositions, we and our collaborators may still be barred from making, using and selling such product candidates or technologies because of the patent rights of others. Others may have filed, and in the future may file, patent applications covering compositions, products or methods that are similar or identical to ours, which could materially affect our ability to successfully develop any product candidates or to successfully commercialize any approved products alone or with collaborators. In addition, because patent applications can take many years to issue, there may be currently pending applications unknown to us that may later result in issued patents that we or our collaborators may infringe. These patent applications may have priority over patent applications filed by us.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our owned and licensed 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 technology and products, or limit the duration of the patent protection of our technology and products. For example, in August 2019, the PTAB, of the United States Patent and Trademark Office, or the USPTO, initiated two patent interferences, administrative proceedings within the USPTO, involving a family of patents that have been issued to us and a pending patent application filed by a third party. An interference is conducted by the PTAB when opposing parties have applied for patent claims to the same invention or substantially the same invention. The interference is conducted to determine which party, if either, is entitled to claims to the subject matter of the interference. In October 2020, we announced the PTAB has issued judgements in our favor in two patent interference proceedings that challenged nine U.S. patents we owned. The patents, which issued in 2018, relate to allogeneic CAR T cells produced by inserting a gene encoding a CAR into the TRAC locus, as well as methods of using those cells for cancer immunotherapy. In the interference proceedings, a third party argued that it had invented the technology in 2012. The PTAB, however, found that the third-party patent application did not satisfy the written description requirement and rejected these claims while maintaining the claims in all nine of our patents. Any adverse outcome in future interference proceedings could affect our competitive position, including, without limitation, loss of some or all of our involved patent claims, limiting our ability to stop others from using or commercializing similar or identical technology and products, which could harm our business, financial condition and results of operations. Protecting our patent rights in connection with such proceeding may also be expensive and may involve the diversion of significant management time.

Furthermore, we cannot guarantee that any patents will be issued from any pending or future owned or licensed patent applications. Thus, even if our patent applications issue as patents, they may not issue in a form that will provide us with meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. In addition, third parties may be able to develop products that are similar to, or better than, ours in a way that is not covered by the claims of our patents, or may have blocking patents that could prevent us from marketing our products or practicing our own patented technology. Moreover, patents have a limited lifespan. In the United States, the natural expiration of a patent is generally 20 years after it is filed. Various extensions may be available; however the life of a patent, and the protection it affords, is limited. Without patent protection for current or future product candidates, we may be open to competition from generic versions of such potential products. Given the amount of time

required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such 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 those we or our collaborators may develop.

Obtaining and maintaining a patent portfolio entails significant expense, including periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and patent applications. These expenditures can be at numerous stages of prosecuting patent applications and over the lifetime of maintaining and enforcing issued patents. We may or may not choose to pursue or maintain protection for particular intellectual property in our portfolio. If we choose to forgo patent protection or to allow a patent application or patent to lapse purposefully or inadvertently, our competitive position could suffer. There are situations, however, in which failure to make certain payments or noncompliance with certain requirements in the patent process can result in abandonment or lapse of a 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, which would have a material adverse effect on our business.

Legal action that may be required to enforce our patent rights can be expensive and may involve the diversion of significant management time. There can be no assurance that we will have sufficient financial or other resources to file and pursue infringement claims, which typically last for years before they are concluded. In addition, these legal actions could be unsuccessful and result in the invalidation of our patents, a finding that they are unenforceable or a requirement that we enter into a licensing agreement with or pay monies to a third party for use of technology covered by our patents. We may or may not choose to pursue litigation or other actions against those that have infringed on our patents, or have used them without authorization, due to the associated expense and time commitment of monitoring these activities. If we fail to successfully protect or enforce our intellectual property rights, our competitive position could suffer, which could harm our results of operations.

Many biotechnology companies and academic institutions are currently pursuing a variety of different nuclease systems for genome editing technologies using zinc finger nucleases, TALENs, and clustered regularly interspaced short palindromic repeats associated protein-9 nuclease, or CRISPR/Cas9, and the use of those nucleases in cancer immunotherapy, gene therapy and genome editing. Although those nucleases are physically and chemically different from our ARCUS nucleases, those companies and institutions may seek patents that broadly cover aspects of cancer immunotherapy, gene therapy and genome editing using nucleases generally. Such patents, if issued, valid and enforceable, could prevent us from marketing our product candidates, if approved, practicing our own patented technology, or might require us to take a license which might not be available on commercially reasonable terms or at all. While we expect that we will continue to be able to patent our ARCUS nucleases for the foreseeable future, as the scientific and patent literature relating to engineered endonucleases increases, including our own patents and publications, it may become more difficult or impossible to patent new engineered endonucleases in the future.

If we fail to comply with our obligations in the agreements under which we license intellectual property rights from third parties or otherwise experience disruptions to our business relationships with our licensors, we could lose license rights that are important to our business.

We are a party to a number of intellectual property license agreements that are important to our business and expect to enter into additional license agreements in the future. Our existing license agreements impose, and we expect that future license agreements will impose, various diligence, milestone payment, royalty and other obligations on us. We may need to outsource and rely on third parties for many aspects of the development, sales and marketing of any products covered under our current and future license agreements. Delay or failure by these third parties could adversely affect the continuation of our license agreements with our licensors. If we fail to comply with any of our obligations under these agreements, or we are subject to a bankruptcy, our licensors may have the right to terminate the license, in which event we would not be able to market any products covered by the license.

In addition, disputes may arise regarding the payment of the royalties due to licensors in connection with our exploitation of the rights we license from them. Licensors may contest the basis of royalties we retained and claim that we are obligated to make payments under a broader basis. In addition to the costs of any litigation we may face as a result, any legal action against us could increase our payment obligations under the respective agreement and require us to pay interest and potentially damages to such licensors.

In some cases, patent prosecution of our licensed technology is controlled solely by the licensor. If such licensor fails to obtain and maintain patent or other protection for the proprietary intellectual property we license from such licensor, we could lose our rights to such intellectual property or the exclusivity of such rights, and our competitors could market competing products using such intellectual property. In that event, we may be required to expend significant time and resources to develop or license replacement technology. If we are unable to do so, we or our collaborators may be unable to develop or commercialize the affected product candidates, which could harm our business significantly. In other cases, we control the prosecution of patents resulting from licensed technology. In the event we breach any of our obligations related to such prosecution, we may incur significant liability to our licensing partners.

For example, our license agreement with Duke University, or Duke, which we refer to as the Duke License, imposes various payment, royalty and other obligations on us in order to maintain the license. If we fail to make royalty payments or milestone payments required under the Duke License, Duke may terminate the agreement. If we or our affiliates obtain a license from a third party to practice the Duke technology, we must use commercially reasonable efforts to secure a covenant not to sue Duke, or any of its faculty, students, employees or agents, for any research and development efforts conducted at Duke that resulted in the creation of any of its inventions or intellectual property rights arising therefrom. Additionally, because development of the Duke technology was funded in part by the U.S. government, it is subject to certain government rights and obligations, including the requirement that any products sold in the United States based upon such technology be substantially manufactured in the United States.

In addition, our cross-license agreement with Cellectis, or the Cellectis License, imposes various obligations on us in order to maintain the license. In particular, if we participate in or provide assistance to a third party challenging the validity, enforceability and/or patentability of any claim of any patent licensed to us by Cellectis under this agreement, Cellectis may terminate the agreement. The Cellectis License does not provide exclusive rights to use the licensed intellectual property and technology or rights in all relevant fields in which we may wish to develop or commercialize our technology and products in the future. As a result, we are not able to prevent competitors from developing and commercializing competitive products and technology that may use this technology. Additionally, we do not have the right to control the preparation, filing, prosecution, maintenance, enforcement and defense of patents and patent applications covering the technology that we license from Cellectis. Therefore, we cannot be certain that these patents and patent applications will be prepared, filed, prosecuted, maintained and defended in a manner consistent with the best interests of our business. If Cellectis or other licensors fail to prosecute, maintain, enforce and defend the patents subject to such licenses, or lose rights to those patents or patent applications, the rights we have licensed may be reduced or eliminated, and our right to develop and commercialize any of our products that are the subject of such licensed rights could be adversely affected.

If we fail to comply with our obligations under the Duke License or the Cellectis License, or arrangements with any other licensors, our counterparties may have the right to terminate these agreements, in which event we might not be able to develop, manufacture or market any product candidate that is covered by these agreements, which could materially adversely affect the value of any such product candidate. Termination of these agreements or reduction or elimination of our rights under these agreements may result in our having to negotiate new or reinstated agreements with less favorable terms, or cause us to lose our rights under these agreements, including our rights to important intellectual property or technology.

Disputes may arise regarding intellectual property subject to a license agreement, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- the amounts of royalties, milestones or other payments due to our licensors;
- the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the license 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 ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our collaborators; and
- the priority of invention of patented technology.

Such disputes may be costly to resolve and may divert management's attention away from day-to-day activities. If disputes over intellectual property that we have licensed from third parties prevent or impair our ability to maintain our licensing arrangements on acceptable terms, we or our collaborators may be unable to successfully develop and commercialize the affected product candidates.

Some of our in-licensed intellectual property has been discovered through government funded research and thus may be subject to federal regulations such as "march-in" rights, certain reporting requirements and a preference for U.S.-based companies, and compliance with such regulations may limit our exclusive rights and our ability to contract with non-U.S. manufacturers.

Certain intellectual property rights that have been in-licensed pursuant to the Duke License have been generated through the use of U.S. government funding and are therefore subject to certain federal regulations. As a result, the U.S. government may have certain rights to intellectual property embodied in our current or future product candidates pursuant to the Bayh-Dole Act of 1980, or the Patent and Trademark Law Amendment. These U.S. government rights include a non-exclusive, non-transferable, irrevocable worldwide license to use inventions for any governmental purpose. In addition, the U.S. government has the right, under certain limited circumstances, to require the licensor to grant exclusive, partially exclusive or non-exclusive licenses to any of these inventions to a third party if it determines that (1) adequate steps have not been taken to commercialize the invention, (2) government action is necessary to meet public health or safety needs or (3) government action is necessary to meet requirements for public use

under federal regulations (also referred to as "march-in rights"). The U.S. government also has the right to take title to these inventions if the licensor fails to disclose the invention to the government or fails to file an application to register the intellectual property within specified time limits. Intellectual property generated under a government funded program is also subject to certain reporting requirements, compliance with which may require us to expend substantial resources. In addition, the U.S. government requires that any products embodying any of these inventions or produced through the use of any of these inventions be manufactured substantially in the United States, and the Duke License requires that we comply with this requirement. This preference for U.S. industry may be waived by the federal agency that provided the funding if the owner or assignee of the intellectual property can show that reasonable but unsuccessful efforts have been made to grant licenses on similar terms to potential licensees that would be likely to manufacture the products substantially in the United States or that under the circumstances domestic manufacture is not commercially feasible. This preference for U.S. industry may limit our ability to contract with non-U.S. product manufacturers for products covered by such intellectual property. To the extent any of our owned or licensed future intellectual property is also generated through the use of U.S. government funding, the provisions of the Bayh-Dole Act may similarly apply.

If we do not obtain patent term extension in the United States under the Hatch-Waxman Act and in foreign countries under similar legislation with respect to our product candidates, thereby potentially extending the term of marketing exclusivity for such product candidates, our business may be harmed.

In the United States, a patent that covers an FDA-approved drug or biologic may be eligible for a term extension designed to restore the period of the patent term that is lost during the premarket regulatory review process conducted by the FDA. Depending upon the timing, duration and conditions of FDA marketing approval of our product candidates, one or more of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act, which permits a patent term extension of up to five years for a patent covering an approved product as compensation for effective patent term lost during product development and the FDA regulatory review process. In the European Union, our product candidates may be eligible for term extensions based on similar legislation. In either jurisdiction, however, we may not receive an extension if we fail to apply within applicable deadlines, fail to apply prior to expiration of relevant patents or otherwise fail to satisfy applicable requirements. Even if we are granted such extension, the duration of such extension may be less than our request. If we are unable to obtain a patent term extension, or if the term of any such extension is less than our request, the period during which we can enforce our patent rights for that product will be in effect shortened and our competitors may obtain approval to market competing products sooner. The resulting reduction of years of revenue from applicable products could be substantial.

Patents and patent applications involve highly complex legal and factual questions, which, if determined adversely to us, could negatively impact our patent position.

The patent positions of biopharmaceutical and biotechnology companies and other actors in our fields of business can be highly uncertain and typically involve complex scientific, legal and factual analyses. In particular, the interpretation and breadth of claims allowed in some patents covering biopharmaceutical compositions may be uncertain and difficult to determine, and are often affected materially by the facts and circumstances that pertain to the patented compositions and the related patent claims. The standards of the USPTO and its foreign counterparts are sometimes uncertain and could change in the future. Consequently, the issuance and scope of patents cannot be predicted with certainty. Patents, if issued, may be challenged, invalidated or circumvented. U.S. patents and patent applications may also be subject to interference or derivation proceedings, and U.S. patents may be subject to reexamination proceedings, post-grant review and/or *inter partes* review in the USPTO. International patents may also be subject to opposition or comparable proceedings in the corresponding international patent office, which could result in either loss of the patent or denial of the patent application or loss or reduction in the scope of one or more of the claims of the patent or patent application. In addition, such interference, derivation, reexamination, post-grant review, *inter partes* review and opposition proceedings may be costly. Accordingly, rights under any issued patents may not provide us with sufficient protection against competitive products or processes.

Furthermore, even if not challenged, our patents and patent applications may not adequately protect our technology and any product candidates or products that we develop alone or with collaborators or prevent others from designing their products to avoid being covered by our claims. If the breadth or strength of protection provided by the patent applications we hold with respect to product candidates or potential products is threatened, it could dissuade companies from collaborating with us to develop, and could threaten our or their ability to successfully commercialize, such product candidates. Furthermore, for U.S. applications in which any claim is entitled to a priority date before March 16, 2013, an interference proceeding can be provoked by a third party or instituted by the USPTO in order to determine who was the first to invent any of the subject matter covered by such patent claims.

In addition, changes in, or different interpretations of, patent laws in the United States and other countries may permit others to use our discoveries or to develop and commercialize our technology and product candidates or products without providing any compensation to us, or may limit the scope of patent protection that we are able to obtain. The laws of some countries do not protect intellectual property rights to the same extent as U.S. laws, and those countries may lack adequate rules and procedures for defending our intellectual property rights.

If the patent applications we hold or have in-licensed with respect to our current and future research and development programs and product candidates fail to issue, if their validity, breadth or strength of protection is threatened, or if they fail to provide meaningful exclusivity for our technology or any products and product candidates that we or our collaborators may develop, it could dissuade companies from collaborating with us to develop product candidates, encourage competitors to develop competing products or technologies and threaten our or our collaborators' ability to commercialize future product candidates. Any such outcome could have a material adverse effect on our business.

Third parties may assert claims against us alleging infringement of their patents and proprietary rights, or we may need to become involved in lawsuits to defend or enforce our patents, either of which could result in substantial costs or loss of productivity, delay or prevent the development and commercialization of product candidates, prohibit our use of proprietary technology or sale of potential products or put our patents and other proprietary rights at risk.

Our commercial success depends in part upon our ability to develop, manufacture, market and sell product candidates without alleged or actual infringement, misappropriation or other violation of the patents and proprietary rights of third parties. Litigation relating to infringement or misappropriation of patent and other intellectual property rights in the pharmaceutical, biotechnology and agricultural biotechnology industries is common, including patent infringement lawsuits, interferences, oppositions and reexamination proceedings before the USPTO and corresponding international patent offices. The various markets in which we plan to operate are subject to frequent and extensive litigation regarding patents and other intellectual property rights. In addition, many companies in intellectual property-dependent industries, including the biotechnology, agricultural biotechnology and pharmaceutical industries, have employed intellectual property litigation as a means to gain an advantage over their competitors. Numerous United States, EU and other internationally issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we and our collaborators are developing product candidates, and as the biotechnology, agricultural biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our product candidates may be subject to claims of infringement of the intellectual property rights of third parties. For example, we are aware of certain patents held by third parties relating to the modification of T cells, including the production of CAR T cells. Although conducting clinical trials and other development activities with respect to our CAR T product candidates is not considered an act of infringement in the United States, if and when any of our CAR T product candidates may be approved by the FDA, those third parties may seek to enforce their patents by filing a patent infringement lawsuit against us. As a result of any patent infringement claims, or in order to avoid any potential infringement claims, we may choose to seek, or be required to seek, a license from the third party, which may require payment of substantial royalties or fees, or require us to grant a cross-license under our intellectual property rights, similar to the cross license we granted Cellectis as part of our patent litigation settlement. These licenses may not be available on reasonable terms or at all. Even if a license can be obtained on reasonable terms, the rights may be nonexclusive, which would give our competitors access to the same intellectual property rights. If we are unable to enter into a license on acceptable terms, we or our collaborators could be prevented from commercializing one or more product candidates, or forced to modify such product candidates, or to cease some aspect of our business operations, which could harm our business significantly. We or our collaborators might also be forced to redesign or modify our technology or product candidates so that we no longer infringe the third-party intellectual property rights, which may result in significant cost or delay to us, or which redesign or modification could be impossible or technically infeasible. Even if we were ultimately to prevail, any of these events could require us to divert substantial financial and management resources that we would otherwise be able to devote to our business.

Further, if a patent infringement suit is brought against us, our collaborators or our third-party service providers, our development, manufacturing or sales activities relating to the product or product candidate that is the subject of the suit may be delayed or terminated. In addition, defending such claims has in the past and may in the future cause us to incur substantial expenses and, if successful, could cause us to pay substantial damages if we are found to be infringing a third party's patent rights. These damages potentially include increased damages and attorneys' fees if we are found to have infringed such rights willfully. Some claimants may have substantially greater resources than we do and may be able to sustain the costs of complex intellectual property litigation to a greater degree and for longer periods of time than we could. In addition, patent holding companies that focus solely on extracting royalties and settlements by enforcing patent rights may target us. In addition, if the breadth or strength of protection provided by the patents and patent applications we own or in-license is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

We have been and may in the future be subject to third-party claims and similar adversarial proceedings or litigation in other jurisdictions regarding our infringement of the patent rights of third parties. Even if such claims are without merit, a court of competent jurisdiction could hold that these third-party patents are valid, enforceable and infringed, and the holders of any such patents may be able to block our or our collaborators' ability to further develop or commercialize the applicable product candidate unless we obtain a license under the applicable patents, or until such patents expire or are finally determined to be invalid or unenforceable. Similarly, if any third-party patents were held by a court of competent jurisdiction to cover aspects of our technologies, compositions, formulations, or methods of treatment, prevention or use, the holders of any such patents may be able to prohibit our use of those technologies, compositions, formulations, methods of treatment, prevention or use or other technologies, effectively

blocking our or our collaborators' ability to develop and commercialize the applicable product candidate until such patent expires or is finally determined to be invalid or unenforceable or unless we or our collaborators obtain a license.

Some of our competitors may be able to sustain the costs of complex intellectual property litigation more effectively than we can because they have substantially greater resources. In addition, intellectual property litigation, regardless of its outcome, may cause negative publicity, adversely impact prospective customers, cause product shipment delays or prohibit us from manufacturing, marketing or otherwise commercializing our products, services and technology. Any uncertainties resulting from the initiation and continuation of any litigation could have a material adverse effect on our ability to raise additional funds or otherwise have a material adverse effect on our business, results of operation, financial condition or cash flows.

If we or one of our licensors were to initiate legal proceedings against a third party to enforce a patent covering our technology or a product candidate, the defendant could counterclaim that our patent is invalid or unenforceable. In patent litigation in the United States and Europe, defendant counterclaims alleging invalidity or unenforceability are common. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, for example, lack of novelty, obviousness or non-enablement. Third parties might allege unenforceability of our patents because during prosecution of the patent an individual connected with such prosecution withheld relevant information, or made a misleading statement. The outcome of proceedings involving assertions of invalidity and unenforceability during patent litigation is unpredictable. With respect to the validity of patents, for example, we cannot be certain that there is no invalidating prior art of which we and the patent examiner were unaware during prosecution, but that an adverse third party may identify and submit in support of such assertions of invalidity. If a defendant were to prevail on a legal assertion of invalidity or unenforceability, we would lose at least part, and perhaps all, of the patent protection on our technology or product candidates. Our patents and other intellectual property rights also will not protect our technology if competitors design around our protected technology without infringing our patents or other intellectual property rights. Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses and could distract our technical and management personnel from their normal responsibilities. In addition, 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, and if securities analysts or investors view these announcements in a negative light, the price of our common stock could be adversely affected. Such litigation or proceedings could substantially increase our operating losses and reduce our resources available for development activities. We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings.

Developments in patent law could have a negative impact on our business.

From time to time, the United States Supreme Court, or the Supreme Court, other federal courts, the United States Congress, or Congress, the USPTO and similar international authorities may change the standards of patentability, and any such changes could have a negative impact on our business. For example, the America Invents Act, or the AIA, which was passed in September 2011, resulted in significant changes to the U.S. patent system. An important change introduced by the AIA is that, as of March 16, 2013, the United States transitioned from a "first-to-invent" to a "first-to-file" system for deciding which party should be granted a patent when two or more patent applications are filed by different parties claiming the same invention. Under a "first-to-file" system, assuming the other requirements for patentability are met, the first inventor to file a patent application generally will be entitled to a patent on the invention regardless of whether another inventor had made the invention earlier. A third party that files a patent application in the USPTO after that date but before us could therefore be awarded a patent covering an invention of ours even if we made the invention before it was made by the third party. Circumstances could prevent us from promptly filing patent applications on our inventions.

The AIA limited where a patentee may file a patent infringement suit and provided opportunities for third parties to challenge any issued patent in the USPTO. Those provisions apply to all of our U.S. patents, regardless of when issued. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in U.S. federal courts necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action. Accordingly, a third party may attempt to use the USPTO procedures to invalidate our patent claims that would not have been invalidated if first challenged by the third party as a defendant in a district court action. These provisions could increase the uncertainties and costs surrounding the prosecution of our or our licensors' patent applications and the enforcement or defense of our or our licensors' issued patents.

Additionally, the Supreme Court has ruled on several patent cases in recent years either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations, and there are other open questions under patent law that courts have yet to decisively address. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of our patents and patent applications. Depending on decisions by Congress, the federal courts and the USPTO, the laws and regulations governing patents could change in unpredictable ways and could weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future. In addition, the European patent system is relatively stringent in the type of amendments that are allowed during prosecution, but the complexity and uncertainty of European patent laws has also increased in recent years. Complying with these laws and regulations could limit our ability to obtain new patents in the future that may be important for our business.

If we were unable to protect the confidentiality of our trade secrets and enforce our intellectual property assignment agreements, our business and competitive position would be harmed.

In addition to patent protection, because we operate in the highly technical field of development of product candidates and products using genome editing, we rely significantly on trade secret protection in order to protect our proprietary technology and processes. Trade secrets are difficult to protect. Our policy is to enter into confidentiality and intellectual property assignment agreements with our employees, consultants, outside scientific collaborators, sponsored researchers and other advisors. These agreements generally require that the other party keep confidential and not disclose to third parties all confidential information developed by the party or made known to the party by us during the course of the party's relationship with us. These agreements also generally provide that inventions conceived by the party in the course of rendering services to us will be our exclusive property. However, we may be unsuccessful in executing such an agreement with each party who in fact conceives or develops intellectual property that we regard as our own. Our assignment agreements may not be self-executing or may be breached, and we may be forced to bring claims against third parties, or defend claims they may bring against us, to determine the ownership of what we regard as our intellectual property. In addition, these agreements may be held unenforceable and may not effectively assign intellectual property rights to us. If our trade secrets and other unpatented or unregistered proprietary information are disclosed, we are likely to lose such trade secret protection.

In addition, certain provisions in our intellectual property agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could affect the scope of our rights to the relevant intellectual property or technology, or affect financial or other obligations under the relevant agreement, either of which could have a material adverse effect on our business, financial condition, results of operations and prospects.

In addition, agreements with third parties typically restrict the ability of such third parties to publish data potentially relating to our trade secrets. Our academic collaborators typically have rights to publish data, provided that we are notified in advance and may delay publication for a specified period of time in order to secure our intellectual property rights arising from the arrangement. In other cases, publication rights are controlled exclusively by us, although in some cases we may share these rights with other parties. We also conduct joint research and product development activities that may require us to share trade secrets under the terms of our research and development collaborations or similar agreements. In addition to contractual measures, we try to protect the confidential nature of our proprietary information using physical and technological security measures. Such measures may not provide adequate protection for our proprietary information. For example, our security measures may not prevent an employee or consultant with authorized access from misappropriating our trade secrets and providing them to a competitor, and the recourse we have available against such misconduct may not provide an adequate remedy to protect our interests fully. 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, courts outside the United States may be less willing to protect trade secrets. Furthermore, our proprietary information may be independently developed by others in a manner that could prevent legal recourse by us. Competitors could purchase any products we may develop and commercialize and attempt to reverse engineer and replicate some or all of the competitive advantages we derive from our development efforts, willfully infringe our intellectual property rights or design around our protected technology. In addition, our key employees, consultants, suppliers or other individuals with access to our proprietary technology and know-how may incorporate that technology and know-how into projects and inventions developed independently or with third parties. As a result, disputes may arise regarding the ownership of the proprietary rights to such technology or know-how, and any such dispute may not be resolved in our favor. If any of our confidential or proprietary information, including our trade secrets, were to be disclosed or misappropriated, or if any such information was independently developed by a competitor, our competitive position could be harmed and such disclosure or misappropriation could have a material adverse effect on our business.

We will not seek to protect our intellectual property rights in all jurisdictions throughout the world, and we may not be able to adequately enforce our intellectual property rights even in the jurisdictions where we seek protection.

Filing, prosecuting and defending patents on product candidates in all countries and jurisdictions throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States could be less extensive than those in the United States, assuming that rights are obtained in the United States. In-licensing patents covering product candidates in all countries throughout the world may similarly be prohibitively expensive, if such opportunities are available at all. 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.

We generally apply for patents in those countries where we intend to make, have made, use, offer for sale or sell products and where we assess the risk of infringement to justify the cost of seeking patent protection. However, we do not seek protection in all countries where we sell products and we may not accurately predict all the countries where patent protection would ultimately be desirable. If we fail to timely file a patent application in any such country or major market, we may be precluded from doing so at a later date. Competitors may use our technologies in jurisdictions where we do not pursue and obtain patent protection to develop their own products and may export otherwise infringing products to territories where we have patent protection, but where our ability to enforce our patent rights is not as strong as in the United States. These products may compete with any products that we or our collaborators may develop, and our patents or other intellectual property rights may not be effective or sufficient to prevent such competition.

The laws of some other countries do not protect intellectual property rights to the same extent as the laws of the United States. For example, European patent law restricts the patentability of methods of treatment of the human body more than U.S. law does. Patent protection must ultimately be sought on a country-by-country basis, which is an expensive and time-consuming process with uncertain outcomes. Accordingly, we may choose not to seek patent protection in certain countries, and we will not have the benefit of patent protection in such countries. In addition, the legal systems of some countries, particularly developing countries, do not favor the enforcement of patents and other intellectual property protection, especially those relating to biopharmaceuticals or biotechnologies. As a result, many companies have encountered significant difficulties in protecting and defending intellectual property rights in certain jurisdictions outside the United States. Such issues may make it difficult for us to stop the infringement of our patents, if obtained, or the misappropriation of our other intellectual property rights. For example, many other countries, including countries in the EU, have compulsory licensing laws under which a patent owner must grant licenses to third parties. In addition, many countries limit the enforceability of patents against third parties, including government agencies or government contractors. In these countries, patents may provide limited or no benefit. In those countries, we and our licensors may have limited remedies if patents are infringed or if we or our licensors are compelled to grant a license to a third party, which could materially diminish the value of those patents and could limit our potential revenue opportunities. Accordingly, our and our licensors' efforts to enforce intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we own or license.

Furthermore, proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, subject our patents to the risk of being invalidated or interpreted narrowly, subject our patent applications to the risk of not issuing or 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 to us, if any, may not be commercially meaningful, while the damages and other remedies we may be ordered to pay such third parties may be significant. 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.

We may not be successful in obtaining or maintaining necessary rights to product components and processes for our development pipeline through acquisitions and in-licenses.

We have rights, through licenses from third parties and under patents that we own, to the intellectual property to develop the product candidates we are currently developing alone or with collaborators. Because our programs may involve additional product candidates that may require the use of proprietary rights held by third parties, the growth of our business may depend in part on our ability to acquire, in-license or use these proprietary rights. In addition, product candidates may require specific formulations to work effectively and efficiently, and these rights may be held by others. We may be unable to acquire or in-license any compositions, methods of use, processes or other third-party intellectual property rights from third parties that we identify. The licensing and acquisition of third-party intellectual property rights is a competitive area, and a number of more established companies, or companies that have greater resources than we do, may also be pursuing strategies to license or acquire third-party intellectual property rights that we may consider necessary or attractive to develop or commercialize product candidates. These established companies may have a competitive advantage over us due to their size and greater cash resources and clinical development and commercialization capabilities. We may not be able to successfully complete such negotiations and ultimately acquire the rights to the intellectual property surrounding product candidates that we may seek to acquire.

For example, we sometimes collaborate with academic institutions to accelerate our preclinical research or development under written agreements with these institutions. Typically, these institutions provide us with an option to negotiate a license to any of the institution's rights in technology resulting from the strategic alliance. Regardless of such right of first negotiation, we may be unable to negotiate a license within the specified time frame or under terms that are acceptable to us, and the institution may license such intellectual property rights to third parties, potentially blocking our ability to pursue our development and commercialization plans.

In addition, companies that perceive us to be a competitor may be unwilling to assign or license to us intellectual property rights that we require in order to successfully develop and commercialize potential products. We also may be unable to obtain such a license or assignment on terms that would allow us to make an appropriate return on our investment. In either event, our business and prospects for growth could suffer.

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.

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. We may not be able to protect our rights to our 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 registered trademarks or trademarks that incorporate variations of our unregistered trademarks or trade names. Over the long term, if we are unable to successfully register our trademarks and trade names and 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. Our efforts to enforce or protect our proprietary rights related to trademarks, trade secrets, domain names, copyrights and other intellectual property may be ineffective and could result in substantial costs and diversion of resources and could adversely impact our financial condition or results of operations.

Risks Related to Owning Our Common Stock

We could be subject to securities class action litigation.

In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant to us as a clinical-stage biopharmaceutical company, as our stock price can significantly fluctuate as a result of public announcements regarding the progress of our development efforts for our discovery platform and our product candidates. If we face such litigation, it could result in substantial costs and a diversion of management's attention and resources, which could harm our business.

We do not currently intend to pay dividends on our common stock.

We do not intend to pay any dividends to holders of our common stock for the foreseeable future. We currently intend to invest our future earnings, if any, to fund our growth. In addition, pursuant to our loan and security agreement with PWB we are prohibited from paying cash dividends without the prior written consent of PWB and future debt instruments may materially restrict our ability to pay dividends on our common stock. Therefore, you are not likely to receive any dividends on your common stock for the foreseeable future, and the success of an investment in our common stock will depend upon any future appreciation in its value. Consequently, you may need to sell all or part of your common stock after price appreciation, which may never occur, as the only way to realize any future gains on your investment.

Provisions in our amended and restated certificate of incorporation and restated bylaws or Delaware law might discourage, delay or prevent a change in control of our company or changes in our management and therefore depress the trading price of our common stock.

Provisions in our amended and restated certificate of incorporation and our restated bylaws may discourage, delay or prevent a merger, acquisition or other change in control of our company that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions include those establishing:

- a classified board of directors with three-year staggered terms, which may delay the ability of stockholders to change the membership of a majority of our board of directors;
- no cumulative voting in the election of directors, which limits the ability of minority stockholders to elect director candidates;
- the exclusive right of our board of directors to elect a director to fill a vacancy created by the expansion of the board of directors or the resignation, death or removal of a director, which prevents stockholders from filling vacancies on our board of directors;

- the ability of our board of directors to authorize the issuance of shares of preferred stock and to determine the terms of those shares, including preferences and voting rights, without stockholder approval, which could be used to significantly dilute the ownership of a hostile acquirer;
- the ability of our board of directors to alter our bylaws without obtaining stockholder approval;
- the required approval of the holders of at least two-thirds of the shares entitled to vote at an election of directors to adopt, amend or repeal our bylaws or repeal the provisions of our amended and restated certificate of incorporation regarding the election and removal of directors;
- a prohibition on stockholder action by written consent, which forces stockholder action to be taken at an annual or special meeting of our stockholders;
- the requirement that a special meeting of stockholders may be called only by the chairman of the board of directors, our chief executive officer (or our president, in the absence of a chief executive officer) or a majority of our board of directors, which may delay the ability of our stockholders to force consideration of a proposal or to take action, including the removal of directors; and
- advance notice procedures that stockholders must comply with in order to nominate candidates to our board of directors or to propose matters to be acted upon at a stockholders' meeting, which may discourage or deter a potential acquirer from conducting a solicitation of proxies to elect the acquirer's own slate of directors or otherwise attempting to obtain control of us.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the General Corporation Law of the State of Delaware, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner.

Our amended and restated certificate of incorporation and our amended and restated bylaws include exclusive forum provisions for substantially all disputes between us and our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Our amended and restated certificate of incorporation provides that, unless we consent in writing to the selection of an alternative forum to the fullest extent permitted by law, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for (1) any derivative action or proceeding brought on our behalf, (2) any action asserting a claim for breach of a fiduciary duty owed by any of our directors, officers or other employees to us or our stockholders, (3) any action asserting a claim arising pursuant to any provision of the General Corporation Law of the State of Delaware, our amended and restated certificate of incorporation or our amended and restated bylaws, or (4) any action asserting a claim governed by the internal affairs doctrine. Under our amended and restated certificate of incorporation, this exclusive forum provision will not apply to claims which are vested in the exclusive jurisdiction of a court or forum other than the Court of Chancery of the State of Delaware, or for which the Court of Chancery of the State of Delaware does not have subject matter jurisdiction. For instance, the provision would not apply to actions arising under federal securities laws, including suits brought to enforce any liability or duty created by the Exchange Act or the rules and regulations thereunder. Further, our amended and restated bylaws provide that, unless we consent in writing to the selection of an alternative forum, to the fullest extent permitted by law, the federal district courts of the United States will be the exclusive forum for the resolution of any complaint asserting a cause of action arising under the Securities Act and that any person or entity purchasing or otherwise acquiring or holding any interest in shares of our capital stock are deemed to have notice of and consented to this provision. These exclusive forum provisions may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees, which may discourage such lawsuits against us and our directors, officers and other employees. For example, stockholders who do bring a claim in the Court of Chancery could face additional litigation costs in pursuing any such claim, particularly if they do not reside in or near the State of Delaware. The Court of Chancery may also reach different judgments or results than would other courts, including courts where a stockholder considering an action may be located or would otherwise choose to bring the action, and such judgments or results may be more favorable to us than to our stockholders.

We are an "emerging growth company" and a "smaller reporting company," and the reduced disclosure requirements applicable to emerging growth companies and smaller reporting companies may make our common stock less attractive to investors.

We are an "emerging growth company," as defined in the JOBS Act. We will remain an emerging growth company until the earlier of (1) December 31, 2024, (2) the last day of the fiscal year in which we have total annual gross revenue of $1.07 billion or more, (3) the date on which we have issued more than $1.0 billion in nonconvertible debt during the previous three years, or (4) the date on which we are deemed to be a large accelerated filer under the rules of the SEC which means the market value of our common stock that is held by non-affiliates exceeds $700 million as of the prior June 30th. For so long as we remain an emerging growth company, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include:

- being permitted to present only two years of "Management's Discussion and Analysis of Financial Condition and Results of Operations" disclosure in this Annual Report on Form 10-K;
- not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, as amended;
- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements;
- reduced disclosure obligations in our SEC filings regarding executive compensation; and
- exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved.

In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This allows an emerging growth company to delay the adoption of these accounting standards until they would otherwise apply to private companies. We have elected to take advantage of this extended transition period.

We are also a smaller reporting company, and we will remain a smaller reporting company until the fiscal year following the determination that our voting and non-voting common stock held by non-affiliates is more than $250 million measured on the last business day of our second fiscal quarter, or our annual revenues are more than $100 million during the most recently completed fiscal year and our voting and non-voting common stock held by non-affiliates is more than $700 million measured on the last business day of our second fiscal quarter. Similar to emerging growth companies, smaller reporting companies are able to provide simplified executive compensation disclosure and have certain other reduced disclosure obligations, including, among other things, being required to provide only two years of audited financial statements and not being required to provide selected financial data, supplemental financial information or risk factors.

We may choose to take advantage of some, but not all, of the available exemptions for emerging growth companies and smaller reporting companies. We cannot predict whether investors will find our common stock less attractive if we rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be reduced or more volatile.

General Risk Factors

We or third parties with whom we have relationships may be adversely affected by natural or manmade disasters, public health emergencies and other natural catastrophic events, and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.

Natural or manmade disasters could severely disrupt our operations and have a material adverse effect on our business, results of operations, financial condition and prospects. If a natural disaster, public health emergency, power outage or other event occurred that prevented us from using all or a significant portion of our facilities, that damaged our infrastructure 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, and our research and development activities could be setback or delayed. The disaster recovery and business continuity plans we have in place may prove inadequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which could have a material adverse effect on our business, and such an event could disrupt our operations, cause us to incur remediation costs, damage our reputation and cause a loss of confidence in us and our or third parties' ability to conduct clinical trials, which could adversely affect our reputation and delay our research and development programs.

Unstable market and economic conditions may have serious adverse consequences on our business, financial condition and stock price.

Global credit and financial markets have experienced extreme volatility and disruptions in the past several years, including severely diminished liquidity and credit availability, declines in consumer confidence, declines in economic growth, increases in unemployment rates and uncertainty about economic stability, and similar deterioration in the credit and financial markets and confidence in economic conditions may occur in the future. Our general business strategy may be adversely affected by any such economic downturn, volatile business environment or unpredictable and unstable market conditions. If the current equity and credit markets deteriorate, or do not improve, it may make any necessary debt or equity financing more difficult, more costly and more dilutive. Failure to secure any necessary financing in a timely manner and on favorable terms could have a material adverse effect on our growth strategy, financial performance and stock price and could require us to delay or abandon clinical development plans. In addition, there is a risk that one or more of our current service providers, manufacturers or others with whom we have strategic relationships may not survive any difficult economic times, which could directly affect our ability to attain our operating goals.

As of December 31, 2020, we had cash and cash equivalents of $89.8 million. In January 2021, we received an upfront cash payment of $100.0 million and equity investment of $35.0 million in connection with the closing of the Development and License agreement with Lilly. While we are not aware of any downgrades, material losses or other significant deterioration in the fair value of our cash equivalents since December 31, 2020, deterioration of the global credit and financial markets could negatively impact our current portfolio of cash equivalents or our ability to meet our financing objectives. Furthermore, our stock price may decline due in part to the volatility of the stock market and any general economic downturn.

The market price of our common stock may be volatile and fluctuate substantially, which could result in substantial losses for purchasers of our common stock.

The market price of our common stock is likely to be highly volatile and may fluctuate substantially due to many factors, including:

- inconsistent trading volume levels of our common stock;
- announcements or expectations regarding debt or equity financing efforts;
- sales of common stock by us, our insiders or our other stockholders;
- actual or anticipated fluctuations in our financial condition and operating results;
- failure to meet or exceed financial estimates and projections of the investment community or that we provide to the public;
- results from or delays in our studies or trials, or those of our collaborators, competitors or companies perceived to be similar to us;
- delay, failure or discontinuation of any of our product development and research programs, or those of our collaborators, competitors or companies perceived to be similar to us;
- announcements about new research programs or product candidates from us or our collaborators, our competitors or companies perceived to be similar to us;
- announcements by us, our collaborators, our competitors or companies perceived to be similar to us relating to significant acquisitions, strategic partnerships or alliances, joint ventures, collaborations or capital commitments;
- actual or anticipated changes in our growth rate relative to our competitors or companies perceived to be similar to us;
- fluctuations in the valuation of our collaborators, our competitors or companies perceived to be comparable to us;
- a lack of, limited or withdrawal of coverage by security analysts, or positive or negative recommendations by them;
- actual or expected changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- publication of research reports about us, genome editing or the biopharmaceutical and agricultural biotechnology industries;
- developments or changing views regarding the use of genomic products, including those that involve genome editing;
- our ability to effectively manage our growth;

- the recruitment or departure of key personnel;
- the results of any efforts by us to identify, develop, acquire or in-license additional product candidates, products or technologies;
- unanticipated serious safety concerns related to the use of any of our product candidates, or those of our competitors or companies perceived to be similar to us;
- the termination of a collaboration agreement, licensing agreement or other strategic arrangement or the inability to establish additional strategic arrangements on favorable terms, or at all;
- regulatory actions with respect to any of our product candidates, or those of our competitors or companies perceived to be similar to us;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- regulatory or legal developments in the United States and other countries;
- changes in physician, hospital, healthcare provider or agricultural practices that may make our or our collaborators' products less useful;
- changes in the structure of healthcare payment systems;
- significant lawsuits, such as products liability, patent or stockholder litigation;
- short sales of our common stock; and
- general economic, industry and market conditions.

These and other market and industry factors may cause the market price and demand for our common stock to fluctuate substantially, regardless of our actual operating performance. These factors may have a material adverse effect on the market price and liquidity of our common stock, which may limit or prevent you from readily selling your shares of common stock and may affect our ability to obtain financing or enter into desired strategic relationships.

If securities or industry analysts issue an adverse or misleading opinion regarding our common stock, our stock price and trading volume could decline.

The trading market for our common stock relies in part on the research and reports that industry or securities analysts publish about us or our business. We do not control these analysts. If any of the analysts who cover us issue an adverse or misleading opinion regarding us, our business model, our intellectual property or our stock performance, or if our preclinical studies and clinical trials and operating results fail to meet the expectations of analysts, our stock price would likely decline. If one or more of these analysts ceases coverage of us or fails to publish reports on us regularly, we could lose visibility in the financial markets, which in turn could cause our stock price or trading volume to decline.

Item 1B. Unresolved Staff Comments

None.

Item 2. Properties.

We currently occupy approximately 69,500 square feet of office and laboratory space at our corporate headquarters in Durham, North Carolina under a lease that expires in 2024. We also occupy approximately 15,500 square feet of laboratory and office space used by our wholly owned subsidiary, Elo Life Systems, in Durham, North Carolina under a lease that expires in 2026, and we occupy approximately 33,800 square feet of manufacturing, laboratory and office space used for our Manufacturing Center for Advanced Technologies in Research Triangle Park, North Carolina under a lease that expires in 2027.

Item 3. Legal Proceedings.

From time to time we may be involved in claims and proceedings arising in the course of our business. The outcome of any such claims or proceedings, regardless of the merits, is inherently uncertain. We are not currently party to any material legal proceedings.

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.

Our common stock trades on The Nasdaq Global Select Market under the symbol "DTIL."

Holders of Common Stock

As of March 2, 2021, there were approximately 205 holders of record of our common stock. This number does not include "street name" or beneficial holders, whose shares are held of record by banks, brokers, financial institutions and other nominees.

Dividend Policy

We intend to retain future earnings, if any, to finance the operation and expansion of our business and do not anticipate paying any cash dividends in the foreseeable future. In addition, pursuant to our loan and security agreement with PWB, we are prohibited from paying cash dividends without the prior written consent of PWB and future debt instruments may materially restrict our ability to pay dividends on our common stock. Any future determination related to our dividend policy will be made at the discretion of our board of directors after considering our financial condition, results of operations, capital requirements, business prospects and other factors our board of directors deems relevant, and subject to any restrictions applicable to us contained in any future financing instruments.

Item 6. Selected Financial Data.

Not applicable.

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations.

The following discussion and analysis of our financial condition and results of operations should be read in conjunction with our consolidated financial statements and the related notes to those statements included elsewhere in this Annual Report on Form 10-K. Some of the information contained in this discussion and analysis or set forth elsewhere in this Annual Report on Form 10-K, including information with respect to our plans and strategy for our business, includes forward-looking statements that involve risks and uncertainties. As a result of many important factors, including those set forth in Part I. Item 1A. "Risk Factors" of this Annual Report on Form 10-K, our actual results could differ materially from the results described in, or implied by, these forward-looking statements. As used in this Annual Report on Form 10-K, unless the context otherwise requires, references to "we," "us," "our," "the Company" and "Precision" refer to Precision BioSciences, Inc. and its subsidiaries on a consolidated basis.

Overview

We are a life sciences company dedicated to improving life through the application of our pioneering, proprietary ARCUS genome editing platform. We leverage ARCUS in the development of our product candidates, which are designed to treat human diseases and create healthy and sustainable food and agricultural solutions. We are actively developing product candidates in three innovative areas: allogeneic CAR T cell immunotherapy, in vivo gene correction, and food. We are currently conducting a Phase 1/2a clinical trial of PBCAR0191 in adult patients with relapsed or refractory, or R/R, non-Hodgkin lymphoma, or NHL, or R/R B-cell precursor acute lymphoblastic leukemia, or B-ALL. PBCAR0191 is our first gene-edited allogeneic chimeric antigen receptor, or CAR, T cell therapy candidate targeting CD19 and is being developed in collaboration with Servier pursuant to the Servier Agreement. We have received orphan drug designation for PBCAR0191 from the U.S. Food and Drug Administration ("FDA"), for the treatment of acute lymphoblastic leukemia, or ALL. In August 2020, the FDA granted Fast Track Designation for PBCAR0191 for the treatment of B-ALL. The NHL cohort will include patients with mantle cell lymphoma ("MCL"), an aggressive subtype of NHL, for which we have received orphan drug designation from the FDA. Made from donor-derived T cells modified using our ARCUS genome editing technology, PBCAR0191 recognizes the well characterized tumor cell surface protein CD19, an important and validated target in several B-cell cancers, and is designed to avoid graft-versus-host disease, or GvHD, a significant complication associated with donor-derived, cell-based therapies. We believe that this trial, which is designed to assess the safety and tolerability of PBCAR0191 at increasing dose levels, as well as to evaluate anti-tumor activity, is the first U.S.-based clinical trial to evaluate an allogeneic CAR T therapy for R/R NHL. Furthermore, we believe that our proprietary, one-step engineering process for producing allogeneic CAR T cells with a potentially optimized cell phenotype, at large scale in a cost-effective manner, will enable us to overcome the fundamental clinical and manufacturing challenges that have limited the CAR T field to date. We expect to report updated interim data for the PBCAR0191 study in mid-year 2021.

In April 2020, we commenced patient dosing in a Phase 1/2a clinical trial with our second allogeneic CAR T cell therapy product candidate, PBCAR20A. PBCAR20A is wholly owned by us and targets the validated tumor cell surface target CD20. It is being investigated in R/R NHL, including those with R/R chronic lymphocytic leukemia, CLL, or R/R small lymphocytic lymphoma, or SLL. A subset of the NHL patients will have the diagnosis of MCL and we have received orphan drug designation for PBCAR20A from the FDA for the treatment of this disease. Based on the safety profile observed to date with PBCAR0191, the FDA allowed us to commence dosing with PBCAR20A directly at 1 x 10^6 cells/kg. The study has continued to escalate through dose level two (3 x 10^6 cells/kg), and, in February 2021, we commenced patient dosing at dose level 3 (480 x 10^6 cell fixed dose) with a max dose of 6 x 10^6 cells/kg. We expect to report interim data for the PBCAR20A study in 2021.

In June 2020, we commenced patient dosing in a Phase 1/2a clinical trial with our third allogenic CAR T cell therapy product candidate, PBCAR269A. The starting dose of PBCAR269A is 6 x 10^5 cells/kg. PBCAR269A is wholly owned by us and is designed to target the validated tumor cell surface target BCMA. It is being investigated in subjects with R/R multiple myeloma and we have received orphan drug designation and Fast Track Designation from the FDA for this indication. In September 2020, we announced that we entered into a clinical trial collaboration with SpringWorks, a clinical-stage biopharmaceutical company focused on developing medicines for patients with severe rare diseases and cancer. Pursuant to the collaboration, PBCAR269A will be evaluated in combination with nirogacestat, SpringWorks' investigational GSI, in patients with R/R multiple myeloma, which is expected to commence in the first half of 2021. In February 2021, we commenced patient dosing at the highest dose cohort, dose level 3 of 6 x 10^6 cells/kg and we expect to report interim data on the PBCAR269A trial in 2021.

Additionally, in June 2020, Elo, our wholly-owned subsidiary, established a strategic partnership with the Dole and entered into a Research, Development, and Commercialization Agreement with Dole, with the aim to co-develop banana varieties resistant to Foc TR4, utilizing proprietary computational biology workflows and the ARCUS genome editing platform. The disease caused by Foc TR4, commonly known as Fusarium wilt, threatens the continued cultivation of the world's most popular variety of banana called Cavendish, which is of considerable economic significance as this variety is used to produce export bananas for key markets around the globe and Dole is one of the largest producers in the industry. Fungicides, or other traditional means of disease control have failed as the pandemic continues to spread across vital banana growing economies.

In September 2020, we regained full clinical development and commercialization rights, and all data we generated for the *in vivo* chronic HBV program developed under our 2018 collaboration agreement with Gilead Sciences. We are exploring partnership or alternative opportunities to enable the continued development of ARCUS-based HBV therapies.

In October 2020, we announced the U.S. Patent and Trademark Office's PTAB issued judgements in our favor in two patent interference proceedings that challenged nine U.S. patents we owned. The patents, which issued in 2018, relate to allogeneic CAR T cells produced by inserting a gene encoding a CAR into the TRAC locus, as well as methods of using those cells for cancer immunotherapy. In the interference proceedings, a third party argued that it had invented the technology in 2012. The PTAB, however, found that the third-party patent application did not satisfy the written description requirement and rejected these claims while maintaining the claims in all nine of our patents.

In November 2020, we announced a research collaboration and exclusive license agreement with Lilly to utilize ARCUS for the research and development of potential *in vivo* therapies for genetic disorders, with an initial focus on DMD and two other undisclosed gene targets. Under the agreement, Lilly has the right to nominate up to three additional gene targets for genetic disorders over the first four years of the Development and License Agreement, which may be extended to six years upon Lilly's election and payment of an extension fee.

In December 2020, we announced interim clinical results from our Phase 1/2a study of PBCAR0191 as a treatment of R/R NHL and R/R B-ALL. As of the November 16, 2020 cutoff, 27 patients including 16 patients with aggressive NHL and 11 patients with aggressive B-ALL were enrolled and evaluated. In this dose escalation and dose expansion study, PBCAR0191 had an acceptable safety profile with no cases of graft versus host disease, no cases of Grade ≥ 3 cytokine release syndrome, and no cases of Grade ≥ 3 neurotoxicity. PBCAR0191 demonstrated longest durability of response to 11 months in B-ALL. PBCAR0191 with eLD resulted in objective response rate of 83% (5/6) in NHL and B-ALL as compared to 33% (3/9) in NHL with sLD.

Additionally, in December 2020, researchers at Elo in collaboration with Alan Chambers, Ph.D., and the Tropical Research and Education Center at the University of Florida published a paper in *Nature Food*, reporting a chromosome-scale, phased *Vanilla planifolia* genome, which revealed sequence variants for genes that may impact the vanillin pathway, and therefore influence bean quality, including its productivity, flower anatomy, and disease resistance.

In January 2021, we announced that the FDA has accepted our IND application for PBCAR19B, our next-generation, stealth cell, CD19 allogenic CAR T candidate for Non-Hodgkin Lymphoma, and we expect to begin the Phase 1 study by mid-2021. Additionally, in January 2021, we announced that we received a Notice of Allowance from the U.S. Patent and Trademark Office for a patent application covering PBCAR19B. The allowed composition claims of this patent application encompass genetically-modified human T cells comprising the PBCAR19B construct, which is inserted within the T cell receptor alpha constant locus. Once issued, patents arising from this patent family will have standard expiration dates in April 2040. In preclinical studies, PBCAR19B has shown to delay both T cell and natural killer cell mediated allogeneic rejection in vitro and may improve the persistence of allogeneic CAR T cells.

We expect to advance a program targeting the rare genetic disease PH1 as our lead wholly owned *in vivo* gene correction program. PH1 affects approximately 1-3 people per million in the United States and is caused by loss of function mutations in the AGXT gene, leading to the accumulation of calcium oxalate crystals in the kidneys. Patients suffer from painful kidney stones which may ultimately lead to renal failure. Using ARCUS, we are developing a potential therapeutic approach to PH1 that involves knocking out a gene called HAO1 which acts upstream of AGXT. Suppressing HAO1 has been shown in preclinical models by us to prevent the formation of calcium oxalate. We therefore believe that a one-time administration of an ARCUS nuclease targeting HAO1 may be a viable strategy for a durable treatment of PH1 patients. Pre-clinical research has continued to progress, and we expect to provide an update on this program in the first half of 2021.

In January 2021, we disclosed our intention to spinout our wholly owned subsidiary, Elo. We are continuing to explore our strategic options, and the timing of any such sale, spinout or other treatment of Elo remains uncertain.

Since our formation in 2006, we have devoted substantially all of our resources to developing ARCUS, conducting research and development activities, recruiting skilled personnel, developing manufacturing processes, establishing our intellectual property portfolio and providing general and administrative support for these operations. We have financed our operations primarily with proceeds from upfront payments from collaboration and licensing agreements, our IPO, and private placements of convertible preferred stock and convertible debt.

On April 1, 2019, we completed our IPO of 9,085,000 shares of common stock, including the underwriters' full exercise of their option to purchase an additional 1,185,000 additional shares of common stock, at an offering price of $16.00 per share, for net proceeds of approximately $130.5 million after deducting underwriting discounts and commissions and offering expenses payable by us. As of December 31, 2020, we have generated approximately $492.5 million from third parties to date.

Since our inception, we have incurred significant operating losses and have not generated any revenue from the sale of products. Our ability to generate any product revenue or product revenue sufficient to achieve profitability will depend on the successful development and eventual commercialization of one or more of our product candidates or the product candidates of our collaborators for which we may receive milestone payments or royalties. Our net losses were $109.0 million and $92.9 million for the years ended December 31, 2020 and December 31, 2019, respectively. As of December 31, 2020, we had an accumulated deficit of $286.1 million.

We expect our operating expenses to increase substantially in connection with the expansion of our product development programs and capabilities. We will not generate revenue from product sales unless and until we successfully complete clinical development and obtain regulatory approval for one of our product candidates or the product candidates of our collaborators for which we may receive milestone payments or royalties. If we obtain regulatory approval for any of our product candidates, we expect to incur significant expenses related to developing our commercialization capability to support product sales, marketing and distribution. In addition, we expect to continue to incur additional costs associated with operating as a public company.

As a result of these anticipated expenditures, we will need additional financing to support our continuing operations. Until such time as we can generate significant revenue from product sales, if ever, we expect to finance our cash needs through a combination of public equity, debt financings or other sources, which may include current and new collaborations with third parties. Adequate additional financing may not be available to us on acceptable terms, or at all. Our inability to raise capital as and when needed would have a negative impact on our financial condition and our ability to pursue our business strategy. We cannot assure you that we will ever generate significant revenue to achieve profitability.

Because of the numerous risks and uncertainties associated with the development of therapeutic and agricultural products, we are unable to predict the timing or amount of increased expenses or when or if we will be able to achieve or maintain profitability. Even if we are able to generate revenue from product sales, we may not become profitable. If we fail to become profitable or are unable to sustain profitability on a continuing basis, then we may be required to raise additional capital on terms that are unfavorable to us or we may be unable to continue our operations at planned levels and be forced to reduce or terminate our operations.

We currently conduct our operations through two reportable segments: Therapeutics and Food. Our Therapeutics segment is focused on allogeneic CAR T immunotherapy and *in vivo* gene correction. Our Food segment focuses on applying ARCUS to develop food and nutrition products through collaboration agreements with consumer-facing companies.

Impact of COVID-19 Pandemic

We are closely monitoring how the ongoing COVID-19 pandemic continues to affect our employees, business, preclinical studies and clinical trials. The Company has taken steps in line with guidance from the U.S. Centers for Disease Control and Prevention ("CDC") and the State of North Carolina to protect the health and safety of its employees and the community. We have implemented measures to mitigate exposure risks and support operations. We initiated a health and safety program addressing mandatory use of face masks, social distancing, sanitary handwashing practices, use of personal protective equipment stations, stringent cleaning and sanitization of all facilities and measures to reduce total occupancy in facilities. We have also implemented temperature and symptom screening procedures at each location, and we have continuously communicated to all our Precisioneers that if they are not comfortable coming to work, regardless of role, then they do not have to do so. Per guidance from the Cybersecurity & Infrastructure Security Agency, our employees are considered essential workforce and may receive the COVID-19 vaccination as Centers for Disease Control and Prevention defined Group 3 and Group 4.

We are working closely with our clinical sites, physician partners and the patient community to monitor and manage the impact of the evolving COVID-19 pandemic. We remain committed to our clinical programs and development plans, however, disruptions, competing resource demands and safety concerns caused by the COVID-19 pandemic have caused, and are likely to continue to cause delays in our clinical trial site activation and impact our ability to enroll patients. We may also experience other difficulties, disruptions or delays in conducting preclinical studies or initiating, enrolling, conducting or completing our planned and ongoing clinical trials, and we may incur other unforeseen costs as a result. We expect that the COVID-19 pandemic may continue to impact our business, including our preclinical studies and clinical trials. At this time, there is still significant uncertainty relating to the trajectory of the COVID-19 pandemic and impact of related responses. The impact of COVID-19 on our preclinical studies and any further impact to our clinical trials will largely depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the ultimate geographic spread of the disease, the duration of the pandemic, travel restrictions and social distancing in the United States and other countries, business closures or business disruptions, the ultimate impact of COVID-19 on financial markets and the global economy, and the effectiveness of actions taken in the United States and other countries to contain and treat the disease. The Coronavirus, Aid, Relief and Economic Security Act ("CARES Act") was signed into law on March 27, 2020, which provides for, among other things, the deferral of the deposit and payment of certain taxes. Pursuant to the CARES Act, the Company elected to defer payment of the employer's share of social security taxes incurred between May 1, 2020 and December 31, 2020. See "Risk Factors— *The outbreak of the ongoing novel coronavirus disease, COVID-19 has impacted our business, or and*

any other pandemic, epidemic or outbreak of an infectious disease may materially and adversely impact our business, including our preclinical studies and clinical trials." in Part I, Item 1A. of this Annual Report on Form 10-K.

Therapeutics Segment Collaborations

Eli Lilly and Company

In November 2020, we entered into a research collaboration and exclusive license agreement (the "Development and License Agreement") with Lilly to utilize ARCUS for the research and development of potential in vivo therapies for genetic disorders. Lilly has initially nominated DMD and two gene targets for other genetic disorders, and has the right to nominate up to three additional gene targets for genetic disorders over the first four years of the Development and License Agreement (the "Nomination Period"). Lilly may extend the Nomination Period for an additional two years from the date on which such initial Nomination Period ends, upon Lilly's election and payment of an extension fee. Under the terms of the Development and License Agreement, Lilly will receive an exclusive license to research, develop, manufacture and commercialize the resulting licensed products to diagnose, prevent and treat any and all diseases by in vivo gene editing directed against the applicable gene target. The Development and License Agreement provides that we will be responsible for conducting certain pre-clinical research and IND-enabling activities with respect to the gene targets nominated by Lilly to be subject to the collaboration, including manufacture of initial clinical trial material for the first licensed product. Lilly will be responsible for, and must use commercially reasonable efforts with respect to, conducting clinical development and commercialization activities for licensed products resulting from the collaboration, and may engage us for additional clinical and/or initial commercial manufacture of licensed products.

In January 2021, we and Lilly closed the Development and License Agreement following clearance under the Hart-Scott Rodino Antitrust Improvements Act of 1976, as amended (the "HSR Act"). In connection with the closing, we received an upfront cash payment of $100.0 million as well as $35.0 million from Lilly's purchase of 3,762,190 newly issued shares of our common stock pursuant to a stock purchase agreement as described below (the "Stock Purchase Agreement"). We will also be eligible to receive milestone payments of up to an aggregate of $420 million per licensed product as well as nomination fees for additional targets and certain research funding. If licensed products resulting from the collaboration are approved and sold, we will also be entitled to receive tiered royalties ranging from the mid-single digit percentages to the low-teens percentages on world-wide net sales of the licensed products, subject to customary potential reductions. Lilly's obligation to pay royalties to us expires on a country-by-country and licensed product-by-licensed product basis, upon the latest to occur of certain events related to expiration of patents, regulatory exclusivity or a period of ten years following first commercial sale of the licensed product.

We have the right to elect to co-fund the clinical development of one licensed product, which may be selected from among the third or any subsequent licensed products to reach IND filing. If we elect to co-fund such licensed product, we would reimburse Lilly for a portion of the clinical development expenses for such product and, in exchange, each royalty tier with respect to net sales of such licensed product would be increased by a low single digit percentage. During the term of the Development and License Agreement, we may not (and may not license or collaborate with any third party to) research, develop, or commercialize any in vivo gene editing product directed against any gene targets that have been nominated and are subject to the Development and License Agreement.

Unless earlier terminated, the Development and License Agreement will remain in effect on a licensed product-by-licensed product and country-by-country basis until the expiration of a defined royalty term for each licensed product and country. Lilly has the right to terminate the Development and License Agreement for convenience by providing advance notice to us. Either party may terminate the Development and License Agreement (i) for material breach by the other party and a failure to cure such breach within the time period specified in the agreement or (ii) due to a challenge to its patents brought by the other party.

Servier

In February 2016, we entered into the Servier Agreement, pursuant to which we have agreed to develop allogeneic CAR T cell therapies for five unique antigen targets. One target was selected at the agreement's inception. Two additional hematological cancer targets beyond CD19 and two new solid tumor targets were selected in 2020. With the addition of these new targets, we received development milestone payments in 2020 and may be eligible to receive additional development milestone payments in 2021. We may also be eligible to receive option fees, as well as clinical, regulatory and sales milestone payments in addition to royalties on product sales. Upon selection of an antigen target under the agreement, we have agreed to perform early-stage research and development on individual T cell modifications for the selected target, develop the resulting therapeutic product candidates through Phase 1 clinical trials and prepare initial clinical trial material of such product candidates for use in Phase 2 clinical trials.

In October 2020, we entered into Amendment No. 6 to the Servier Agreement, effective as of October 2, 2020 ("Amendment No. 6"). Terms of the Servier Agreement were amended, solely as applicable to PBCAR0191. Under Amendment No. 6, we are required to complete the ongoing Phase 1/2a clinical trial of PBCAR0191 in adult patients with R/R NHL and R/R B-ALL (the "Clinical Trial") for a specified number of patients in the Phase 1 portion of the Clinical Trial and a number of patients to be determined by us in the

Phase 2a portion of the Clinical Trial. We will be solely responsible for all costs and expenses we incur to complete the Clinical Trial, including the production and release of all required clinical trial material.

The results of the Clinical Trial will be used to determine whether specified development milestones have been achieved with respect to PBCAR0191, in which case, specified corresponding development milestone payments are payable by Servier to us. The results of the Clinical Trial will also be used to determine whether Phase 2 readiness has been achieved for PBCAR0191 and Servier may determine whether, subject to payment of a commercial option exercise fee, to exercise its commercial option and proceed with development and commercialization of PBCAR0191. Following completion of the Clinical Trial, we are not obligated to conduct any further development activities under the Servier Agreement with respect to PBCAR0191 unless we otherwise agree to conduct such further development activities.

We received an upfront payment of $105.0 million under the Servier Agreement in 2016. We have the ability to receive total payments, including the upfront payment, option fees and milestone payments, in the aggregate across all five targets, of up to approximately $1.4 billion. This includes up to $1.3 billion in milestone payments, consisting of up to $329.3 million in development milestone payments and up to $925.0 million in commercial milestone payments. We are also entitled to receive tiered royalties ranging from the mid-single digit percentages to the sub-teen percentages on worldwide net sales, subject to potential customary reductions. We also have the right to participate in the development and commercialization of any licensed products resulting from the collaboration through a 50/50 co-development and co-promotion option in the United States, subject to our payment of an option fee, which is exercisable after Servier's commercial option exercise.

Under the Servier Agreement, we recognized $18.0 million and $7.3 million in revenue during the years ended December 31, 2020 and December 31, 2019, respectively. The amount recorded as deferred revenue was $82.9 million and $80.9 million as of December 31, 2020 and December 31, 2019, respectively.

SpringWorks Therapeutics

In September 2020, we entered into a Clinical Trial Collaboration Agreement with SpringWorks. Pursuant to the agreement, PBCAR269A will be evaluated in combination with nirogacestat, SpringWorks' investigational GSI, in patients with R/R multiple myeloma. Under the terms of the agreement, we will bear all costs with the conduct of the clinical trial including providing PBCAR269A for use in the trial, and SpringWorks is responsible for providing nirogacestat at its sole cost and expense.

Gilead

On July 6, 2020, Gilead Sciences ("Gilead") notified us of its termination of the collaboration and license agreement dated September 10, 2018, subsequently amended by Amendment No. 1 dated March 10, 2020 or (the "Gilead Agreement"), to develop genome editing tools using ARCUS to target viral DNA associated with the hepatitis B virus. Pursuant to the termination notice, the Gilead Agreement terminated on September 4, 2020. Upon termination, we regained full rights and all data we generated for the *in vivo* chronic hepatitis B program developed under the Gilead Agreement.

We recognized $3.9 million and $13.3 million in revenue under the Gilead Agreement during the years ended December 31, 2020 and December 31, 2019, respectively, and $1.5 million in deferred revenue as of December 31, 2019. We did not receive any milestone payments under the Gilead Agreement during the years ended December 31, 2020 or December 31, 2019.

Trustees of the University of Pennsylvania

In January 2018, we entered into a research, collaboration and license agreement with the Trustees of the University of Pennsylvania ("Penn") to collaborate on the preclinical development for gene editing products involving the delivery of an ARCUS nuclease. On April 29, 2020, both parties agreed to coordinate a wind-down of all activities in their entirety under the agreement, effective as of June 30, 2020, however, in August 2020 and subsequently in January 2021, both parties agreed to extend certain portions of the agreement until 2022. We will not be required to make termination payments to Penn.

Food Segment Collaborations

Dole Food Company

Through our wholly owned subsidiary, Elo, in June 2020, we entered into a Research, Development, and Commercialization Agreement with Dole with the aim to co-develop banana varieties resistant to Foc TR4, utilizing proprietary computational biology workflows and the ARCUS genome editing platform. The disease caused by Foc TR4, commonly known as Fusarium wilt, threatens the continued cultivation of the world's most popular variety of banana called Cavendish, which is of considerable economic significance as this variety is used to produce export bananas for key markets around the globe and Dole is one of the largest

producers in the industry. Fungicides, or other traditional means of disease control have failed as the pandemic continues to spread across vital banana growing economies. Development of Foc TR4 varieties is critically important to save the banana industry, to protect the livelihoods of millions of banana growers and continue to provide consumers an affordable and nutritious fruit. Under the terms of the collaboration, Dole will fully fund research and development efforts executed by Elo, and Elo is eligible to receive royalties on any commercialized plant product.

Cargill, Inc.

In 2014, through Elo, we and Cargill, Inc. entered into a collaboration to produce ARCUS-optimized canola varieties with significantly lower levels of saturated fatty acids compared to the current levels in greenhouse studies. On July 30, 2020, we and Cargill mutually agreed to terminate the collaboration, effective August 31, 2020.

Components of Our Results of Operations

Revenue

To date, we have not generated any revenue from product sales and do not expect to generate any revenue from product sales in the foreseeable future. We record revenue from collaboration agreements, including amounts related to upfront payments, milestone payments, annual fees for licenses of our intellectual property and research and development funding.

Research and Development Expenses

Research and development expenses consist primarily of costs incurred for our research activities, including our discovery efforts and the development of our product candidates. These include the following:

- salaries, benefits and other related costs, including share-based compensation expense, for personnel engaged in research and development functions;
- expenses incurred under agreements with third parties, including contract research organizations, or CROs, and other third parties that conduct preclinical research and development activities and clinical trials on our behalf;
- costs of developing and scaling our manufacturing process and manufacturing drug products for use in our preclinical studies and ongoing and future clinical trials, including the costs of contract manufacturing organizations, or CMOs, and our MCAT facility that will manufacture our clinical trial material for use in our preclinical studies and ongoing and potential future clinical trials;
- costs of outside consultants, including their fees and related travel expenses;
- costs of laboratory supplies and acquiring, developing and manufacturing preclinical study and clinical trial materials;
- license payments made for intellectual property used in research and development activities; and
- facility-related expenses, which include direct depreciation costs and expenses for rent and maintenance of facilities and other operating costs if specifically identifiable to research activities.

We expense research and development costs as incurred. We track external research and development costs, including the costs of laboratory supplies and services, outsourced research and development, clinical trials, contract manufacturing, laboratory equipment and maintenance and certain other development costs, by product candidate when the program IND application is accepted by the FDA. Internal and external costs associated with infrastructure resources, other research and development costs, facility related costs and depreciation and amortization that are not identifiable to a specific product candidate are included in the platform development and early-stage research expenses category in the table below.

The following table summarizes our research and development expenses by product candidate or development program for the periods presented:

(in thousands)	Years ended December 31, 2020	2019	Change
Direct research and development expenses by product candidate:			
CD19 external development costs	$ 8,586	$ 4,726	$ 3,860
CD20 external development costs	6,660	9,375	(2,715)
BCMA external development costs	3,144	4,928	(1,784)
Platform development and early-stage research expenses:			
Employee-related costs	37,301	26,383	10,918
Laboratory supplies and services	12,225	11,706	519
Outsourced research and development	7,514	12,416	(4,902)
CMOs and research organizations	7,730	1,770	5,960
Laboratory equipment and maintenance	1,412	1,381	31
Facility-related costs	3,354	3,030	324
Depreciation and amortization	7,441	4,186	3,255
Licensing fees	2,415	2,236	179
Other research and development costs	279	279	—
Total research and development expenses	$ 98,061	$ 82,416	$ 15,645

Research and development activities are central to our business model. We expect that our research and development expenses will continue to increase substantially for the foreseeable future and will comprise a larger percentage of our total expenses as we continue our Phase 1/2a clinical trials for our CD19, CD20 and BCMA product candidates, commence our Phase 1 clinical trial of CD19B, and continue to discover and develop additional product candidates.

We cannot determine with certainty the duration and costs of ongoing and future clinical trials of our CD19, CD19B, CD20, and BCMA product candidates, or any other product candidate we may develop or if, when or to what extent we will generate revenue from the commercialization and sale of any product candidate for which we obtain marketing approval. We may never succeed in obtaining marketing approval for any product candidate. The duration, costs and timing of clinical trials and development of our CD19, CD19B, CD20, and BCMA product candidates, and any other our product candidate we may develop will depend on a variety of factors, including:

- the scope, rate of progress, expense and results of clinical trials of our CD19, CD19B, CD20, and BCMA product candidates, as well as of any future clinical trials of other product candidates and other research and development activities that we may conduct;
- increased costs of additional clinical sites to address slowed enrollment due to the impact of COVID-19;
- uncertainties in clinical trial design and patient enrollment rates;
- the actual probability of success for our product candidates, including their safety and efficacy, early clinical data, competition, manufacturing capability and commercial viability;
- significant and changing government regulation and regulatory guidance;
- the timing and receipt of any marketing approvals; and
- the expense of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights.

A change in the outcome of any of these variables with respect to the development of a product candidate could mean a significant change in the costs and timing associated with the development of that product candidate. For example, if the FDA or another regulatory authority were to require us to conduct clinical trials beyond those that we anticipate will be required for the completion of clinical development of a product candidate, or if we experience significant delays in our clinical trials due to slower than expected patient enrollment or other reasons, we would be required to expend significant additional financial resources and time on the completion of clinical development.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries and other related costs, including share-based compensation, for personnel in our executive, finance, business development, operations and administrative functions. General and administrative expenses also include legal fees relating to intellectual property and corporate matters; professional fees for accounting, auditing, tax and consulting services; insurance costs; travel expenses; and facility-related expenses, which include direct depreciation costs and expenses for rent and maintenance of facilities and other operating costs that are not specifically attributable to research activities.

We expect that our general and administrative expenses will increase in the future as we continue research activities and development of product candidates.

Change in Fair Value of Convertible Notes Payable

We elected on issuance to account for the convertible notes payable we issued in March 2019, or the 2019 Notes, at fair value until their settlement. The change in fair value of the 2019 Notes was recognized through the statement of operations. The 2019 Notes settled into 2,921,461 shares of common stock on the closing of our IPO on April 1, 2019.

Interest Expense

Interest expense consists of interest from the 2019 Notes at a rate of 6% per annum.

Interest Income

Interest income consists of interest income earned on our cash and cash equivalents.

Income Taxes

Since our inception in 2006, we have generated cumulative federal and state net operating loss and research and development ("R&D") credit carryforwards for which we have not recorded any net tax benefit due to the uncertainty around utilizing these tax attributes within their respective carryforward periods. As of December 31, 2020, we had federal, state, and foreign net operating loss carryforwards of $172.7 million, $116.5 million, and $0.6 million, respectively, which may be available to offset future taxable income. A portion of the U.S. federal net operating loss carryforwards in the amount of $19.7 million will begin to expire in 2030 while the remaining federal net operating loss carryforwards of $153.0 million carry forward indefinitely. The state net operating loss carryforwards begin to expire in 2025. The foreign net operating losses carryforward indefinitely. As of December 31, 2020, we also had federal research and development tax credit carryforwards of $9.9 million, which begin to expire in 2027, and an amount less than $0.1 million, which begin to expire in 2030. As of December 31, 2020 and December 31, 2019, we had federal Orphan Drug credits of $6.0 million and $1.8 million, respectively, which begin to expire in 2038. As of December 31, 2020, we also have federal contribution carryforwards of $0.2 million, which begin to expire in 2021. We have recorded a full valuation allowance against our net deferred tax assets at each balance sheet date.

On December 22, 2017, the TCJA was signed into United States law. The TCJA includes a number of changes to existing tax law, including, among other things, a permanent reduction in the federal corporate income tax rate from a top marginal tax rate of 35% to a flat rate of 21%, effective as of January 1, 2018, as well as a limitation of the deduction for net operating losses to 80% of annual taxable income and elimination of net operating loss carrybacks, in each case, for losses arising in taxable years beginning after December 31, 2017 (though any such net operating losses may be carried forward indefinitely). The federal tax rate change resulted in a reduction in the gross amount of our deferred tax assets and liabilities recorded as of December 31, 2017, and a corresponding reduction in our valuation allowance. As a result, no income tax expense or benefit was recognized as of the enactment date of the TCJA.

Results of Operations

Comparison of the Years Ended December 31, 2020 and December 31, 2019

The following table summarizes our results of operations for the years ended December 31, 2020 and December 31, 2019, together with the changes in those items in dollars:

(in thousands)	Years ended December 31, 2020	2019	Change
Revenue	$ 24,285	$ 22,238	$ 2,047
Operating expenses:			
Research and development	98,061	82,416	15,645
General and administrative	36,052	27,026	9,026
Total operating expenses	134,113	109,442	24,671
Loss from operations	(109,828)	(87,204)	(22,624)
Other income (expense), net:			
Change in fair value of convertible note payable	—	(9,758)	9,758
Interest expense	—	(182)	182
Interest income	822	4,267	(3,445)
Total other income (expense), net	822	(5,673)	6,495
Net loss	$ (109,006)	$ (92,877)	$ (16,129)

Revenue

Revenue for the year ended December 31, 2020 was $24.3 million, compared to $22.2 million for the year ended December 31, 2019. The increase of $2.1 million in revenue during the year ended December 31, 2020 was primarily the result of a $10.7 million increase in collaboration revenue recognized from Servier in connection with the development milestones achieved and work performed on the new targets under the Servier Agreement, a $0.8 million increase in revenue recognized from food segment partners, partially offset by a $9.5 million decrease in revenue recognized from Gilead due to the termination of the Gilead Agreement.

Research and Development Expenses

(in thousands)	Years ended December 31, 2020	2019	Change
Direct research and development expenses by product candidate:			
CD19 external development costs	$ 8,586	$ 4,726	$ 3,860
CD20 external development costs	6,660	9,375	(2,715)
BCMA external development costs	3,144	4,928	(1,784)
Platform development and early-stage research expenses:			
Employee-related costs	37,301	26,383	10,918
Laboratory supplies and services	12,225	11,706	519
Outsourced research and development	7,514	12,416	(4,902)
CMOs and research organizations	7,730	1,770	5,960
Laboratory equipment and maintenance	1,412	1,381	31
Facility-related costs	3,354	3,030	324
Depreciation and amortization	7,441	4,186	3,255
Licensing fees	2,415	2,236	179
Other research and development costs	279	279	0
Total research and development expenses	$ 98,061	$ 82,416	$ 15,645

Research and development expenses for the year ended December 31, 2020 were $98.1 million, compared to $82.4 million for the year ended December 31, 2019. The increase of $15.7 million was primarily due to a $16.2 million increase in platform development and early-stage research expenses, a $3.9 million increase in direct research and development expenses related to our CD19 program, partially offset by decreases of $2.7 and $1.8 in direct research and development expenses related to our CD20 and BCMA programs, respectively.

The increase in direct research and development expenses for our CD19 program was primarily due to increases in CMO and research organization costs as we continue to enroll additional patients in the Phase 1/2a clinical trial. The decrease in direct research and development expenses for our CD20 and BCMA programs was primarily due to decreases in external CMO costs as we transferred clinical trial material manufacturing activities for CD20 and BCMA in-house to MCAT.

Platform development and early-stage research expenses increased primarily due to a $10.9 million increase in employee-related expense associated with increased headcount to support our technology platform development and manufacturing capabilities, a $6.0 million increase in CMO and research organization expense, primarily related to our planned CD19B clinical trial, a $3.3 million increase in depreciation and amortization expense driven by our higher depreciable asset base during the year ended December 31, 2020, and a $0.3 million increase in facility-related expenses, partially offset by a $4.9 million decrease in outsourced research and development expense in the year ended December 31, 2020 compared to the year ended December 31, 2019.

General and Administrative Expenses

General and administrative expenses were $36.1 million for the year ended December 31, 2020 compared to $27.0 million for the year ended December 31, 2019. The increase of $9.1 million was primarily due to an increase of $4.0 million in employee-related expense as we increased our general and administrative headcount, $2.9 million in consulting fees, and $2.5 million in increased administrative expenses, including insurance, information technology, franchise and property taxes, and costs related to operating as a public company, partially offset by a $0.3 million decrease in bank fees and other general and administrative expenses.

Change in Fair Value of Convertible Notes Payable

We elected on issuance to account for the 2019 Notes at fair value until their settlement. For the year ended December 31, 2019, we recognized $9.8 million of expense as changes in fair value. The 2019 Notes were settled on the closing of the IPO in April 2019.

Interest Expense

Interest expense of $0.2 million for the year ended December 31, 2019 consists of interest from the 2019 Notes at a rate of 6% per annum.

Interest Income

Interest income was $0.8 million for the year ended December 31, 2020 compared to $4.3 million for the year ended December 31, 2019. The decrease of $3.5 million of interest income generated on our cash and cash equivalent balances was the result of lower interest rates and lower cash balances in the year ended December 31, 2020, compared to the year ended December 31, 2019.

Segment Results

The following tables summarize segment revenues and segment operating loss (see Note 13 to our audited consolidated financial statements included elsewhere in this Annual Report on Form 10-K for additional information regarding our segments):

	For the Years Ended December 31,	
(in thousands)	**2020**	**2019**
Revenue:		
Therapeutics	$ 21,863	$ 20,632
Food	2,422	1,606
Total segment revenue	24,285	22,238
Segment operational cash expenditures:		
Therapeutics	$ 71,841	$ 70,059
Food	7,587	6,984
Total segment operational cash expenditures	79,428	77,043
Segment operating loss:		
Therapeutics	$ (49,978)	$ (49,427)
Food	(5,165)	(5,378)
Total segment operating loss	$ (55,143)	$ (54,805)

We evaluate the operating performance of each segment based on segment operating loss. Segment operating loss is derived by deducting operational cash expenditures, net, from GAAP revenue. Operational cash expenditures are cash disbursements made that are specifically identifiable to the reportable segment (including specifically identifiable research and development and property, equipment and software expenditures). The reportable segment operational cash expenditures include cash disbursements for compensation, laboratory supplies, purchases of property, equipment and software and procuring services from CROs, CMOs and research organizations. We do not allocate general operational expenses or non-cash income statement amounts to our reportable segments.

Therapeutics Segment

Revenue for the year ended December 31, 2020 was $21.9 million, compared to $20.6 million for the year ended December 31, 2019. The increase of $1.3 million was the result of a $10.7 increase in collaboration revenue recognized from Servier, partially offset by a $9.5 million decrease in revenue recognized from Gilead due to the termination of the Gilead Agreement. Segment operational cash expenditures for the year ended December 31, 2020 were $71.8 million, compared to $70.1 million for the year ended December 31, 2019. The increase of $1.7 million in operational cash expenditures was primarily due to an increase in employee costs and payments made to service providers for contract manufacturing and clinical trial research, partially offset by a decrease in capital expenditures for fixed assets and a reduction in payments to external vendors for early-stage research. Segment operating loss increased $0.6 million from $49.4 million for the year ended December 31, 2019 to $50.0 million for the year ended December 31, 2020 primarily due to the factors discussed above.

Food Segment

Revenue for the year ended December 31, 2020 was $2.4 million, compared to $1.6 million for the year ended December 31, 2019. The increase of $0.8 million was primarily attributable to $0.8 million from an agreement with a new collaboration partner entered into during the year ended December 31, 2020. Segment operational cash expenditures for the year ended December 31, 2020 were $7.6 million, compared to $7.0 million for the year ended December 31, 2019. The increase of $0.6 million was primarily due to an increase in employee costs and rent payments, partially offset by a decrease in capital expenditures for fixed assets. Segment operating loss decreased $0.2 million from $5.4 million for the year ended December 31, 2019 to $5.2 million for the year ended December 31, 2020 primarily due to the factors discussed above. As discussed above, we are assessing various options with respect to a potential separation of Elo from Precision, which could occur during 2021.

Liquidity and Capital Resources

Since our inception, we have incurred significant operating losses. We expect to incur significant expenses and operating losses for the foreseeable future as we advance the preclinical and clinical development of our product candidates. We expect that our research and development and general and administrative costs will continue to increase, including in connection with conducting preclinical studies and clinical trials for our product candidates, contracting with CROs and CMOs, the addition of laboratory equipment to MCAT in support of preclinical studies and clinical trials, expanding our intellectual property portfolio and providing general and administrative support for our operations. As a result, we will need additional capital to fund our operations, which we may obtain from additional equity or debt financings, collaborations, licensing arrangements or other sources.

There are no assurances that we will be successful in obtaining an adequate level of financing as and when needed to finance our operations on terms acceptable to us or at all, particularly in light of the economic downturn and ongoing uncertainty related to the COVID-19 pandemic. If we are unable to secure adequate additional funding as and when needed, we may have to significantly delay, scale back or discontinue the development and commercialization of one or more product candidates. In addition, the magnitude and duration of the COVID-19 pandemic and its impact on our liquidity and future funding requirements remains uncertain as of the filing date of this Annual Report on Form 10-K, as the pandemic continues to evolve globally. See "Impact of COVID-19 Pandemic" above and "Risk Factors— *The ongoing novel coronavirus disease, COVID-19 has impacted our business and any other pandemic, epidemic or outbreak of an infectious disease may materially and adversely impact our business, including our preclinical studies and clinical trials"* in Part I, Item 1A. of this Annual Report on Form 10-K for a further discussion of the potential impact of the COVID-19 pandemic on our business.

We do not currently have any approved products and have never generated any revenue from product sales. Through the date of filing this Annual Report on Form 10-K, we have financed our operations primarily with proceeds from our IPO, private placements of our convertible preferred stock, convertible debt and common stock, and upfront payments from collaboration and licensing arrangements. As of December 31, 2020, we had raised approximately $492.5 million of proceeds from third parties through a combination of financings including our IPO, preferred stock and convertible note financings, payments under the Servier Agreement, and funding from other strategic alliances and grants. We also currently have an effective shelf registration statement on Form S-3 (No. 333-238857) filed with the SEC on June 1, 2020 (the "Form S-3") under which we may offer from time to time in one or more offerings

any combination of common and preferred stock, debt securities, warrants and units of up to $200.0 million in the aggregate. As of December 31, 2020, we have not sold any securities under our shelf registration statement.

Cash Flows

Our cash and cash equivalents totaled $89.8 million as of December 31, 2020, compared to $180.9 million as of December 31, 2019.

The following table summarizes our sources and uses of cash for the periods presented:

	For the Years Ended December 31,	
(in thousands)	**2020**	**2019**
Net cash used in operating activities	$ (87,386)	$ (71,015)
Net cash used in investing activities	(5,031)	(24,666)
Net cash provided by financing activities	1,329	173,374
Increase (decrease) in cash and cash equivalents	$ (91,088)	$ 77,693

Cash Used in Operating Activities

Our primary use of cash is to fund operating expenses, which consist primarily of research and development and general and administrative expenses. Our losses have resulted from expenses incurred in connection with our research and development activities, including our clinical programs, preclinical development activities, and general and administrative costs associated with our operations. The use of cash in operating activities during the years ended December 31, 2020 and December 31, 2019 resulted from our net loss adjusted for non-cash expenses and changes in working capital.

Cash used in operating activities during the year ended December 31, 2020 was $87.4 million, compared to $71.0 million during the year ended December 31, 2019. The increase in cash used in operating activities in the year ended December 31, 2020 was primarily due to an increase in employee-related costs associated with increased headcount, increased costs related to our clinical programs with our ongoing CD19 Phase 1/2a clinical trial and initiation of Phase 1/2a clinical trials for our CD20 and BCMA product candidates in 2020, an increase in legal fees and an increase in lease payments.

Cash Used in Investing Activities

Cash used in investing activities primarily relates to leasehold additions, equipment and software. Net cash used in investing activities during the year ended December 31, 2020 was $5.0 million, compared to $24.7 million in the year ended December 31, 2019. The decrease in cash used in investing activities during the year ended December 31, 2020 was primarily due to the completion of the build-out of our MCAT facility in Research Triangle Park and other leased facilities in 2019.

Cash Provided by Financing Activities

Net cash provided by financing activities during the year ended December 31, 2020 was $1.3 million, compared to $173.4 million during the year ended December 31, 2019. The higher cash provided by financing activities during the year ended December 31, 2019, compared to the year ended December 31, 2020, was due to proceeds received from our IPO, which closed in April 2019, and proceeds from the 2019 Notes, which were issued in March 2019. Financing activities in the twelve months ended December 31, 2020 related to cash proceeds received from stock option exercise and our employee stock purchase plan.

Debt Obligations

In March 2019, we issued an aggregate principal amount of $39.6 million of 2019 Notes in a private placement transaction. Upon settlement, the change in fair value of the 2019 Notes was $9.8 million and the accrued interest on the 2019 Notes was $0.2 million. Pursuant to their terms, the 2019 Notes were settled in 2,921,461 shares of our common stock upon the closing of our IPO at a settlement price of $13.60 per share, which is equal to 85% of the IPO price per share.

In May 2019, we entered into the Pacific Western Loan Agreement with PWB as amended by the First Amendment to Loan and Security Amendment, effective September 18, 2019, the Second Amendment to Loan and Security Amendment, effective December 3, 2019 (the "Original Agreement"). On June 23, 2020, the Company and PWB entered into the Third Amendment to Loan and Security Agreement (the "Amendment No. 3") to the Original Agreement (as amended, the "Pacific Western Loan Agreement"). The terms of Amendment No. 3 (a) decrease the aggregate principal amount of advances on a revolving line of credit (the "Revolving Line") from $50.0 million to $30.0 million and (b) extend the maturity date of the Revolving Line to June 23, 2022, provided that, if the Company receives aggregate cash proceeds of at least $125.0 million from the issuance of the Company's equity securities and/or

upfront cash proceeds from strategic partnerships on terms and conditions reasonably satisfactory to PWB, the maturity date shall then instead be June 23, 2023. Under the terms of Amendment No. 3, the interest rate increased to a variable annual rate equal to the greater of (a) 2.75% above the Prime Rate (as defined in the Original Agreement), and (b) 6.00%. The Company must also maintain an aggregate balance of unrestricted cash at PWB (not including amounts in certain specified accounts) equal to or greater than $10.0 million.

The Pacific Western Loan Agreement matures on June 23, 2023, as a result of the events discussed in Note 14 to our audited consolidated financial statements included elsewhere in this Annual Report on Form 10-K.

As of the date of this Annual Report on Form 10-K, there have been no borrowings under our Revolving Line, and we are in compliance with the financial covenants under the Pacific Western Loan Agreement.

Funding Requirements

Our operating expenses increased substantially in 2020 and are expected to continue to increase in the future in connection with the continuation of our current clinical trials, planned initiation of additional clinical trials and expected growth in our portfolio.

We believe that our cash and cash equivalents as of December 31, 2020, cash payments received from Lilly in January 2021 in connection with the closing of the Development and License Agreement, expected operational receipts and available credit will allow us to continue its operations into 2023. We have based these estimates on assumptions that may prove to be imprecise, and we could utilize our available capital resources sooner than we expect. Because of the numerous risks and uncertainties associated with research, development and commercialization of pharmaceutical and agricultural products, it is difficult to estimate with certainty the amount of our working capital requirements. Our future funding requirements will depend on many factors, including:

- the progress, costs and results of our clinical development for our CD19, CD19B, CD20, and BCMA programs as we progress clinical trials, including CRO costs;
- the progress, costs and results of our additional research and preclinical development programs;
- the outcome, timing and cost of meeting regulatory requirements established by the FDA and other comparable foreign regulatory authorities;
- the costs and timing of internal process development and manufacturing scale-up activities and contract with CMOs associated with our CD19, CD19B, CD20, and BCMA programs and other programs we advance through preclinical and clinical development;
- our ability to establish and maintain strategic collaborations, licensing or other agreements and the financial terms of such agreements;
- the scope, progress, results and costs of any product candidates that we may derive from ARCUS or any other product candidates we may develop alone or with collaborators;
- the extent to which we in-license or acquire rights to other products, product candidates or technologies;
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and protecting our intellectual property rights and defending against any intellectual property-related claims; and
- the costs and timing of future commercialization activities, including product manufacturing, marketing, sales and distribution, for any product candidates for which we or our collaborators obtain marketing approval.

Until such time, if ever, that we can generate product revenue sufficient to achieve profitability, we expect to finance our cash needs through a combination of public or private equity or debt financings, collaboration agreements, other third-party funding, strategic alliances, licensing arrangements and marketing and/or distribution arrangements.

To the extent that we raise additional capital through the sale of equity or convertible debt securities, shareholders' ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our shareholders. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise additional funds through other third-party funding, collaboration agreements, strategic alliances, licensing arrangements or marketing and distribution arrangements, we may have to relinquish valuable rights to our technologies, future revenue streams, product development and research programs or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market products or product candidates that we would otherwise prefer to develop and market ourselves.

Contractual Obligations

The following is a summary of our contractual obligations and commitments as of December 31, 2020:

	Payments Due by Period				
(in thousands)	Total[2][3]	Less Than 1 Year	1-3 Years	3-5 Years	More than 5 Years
Lease Obligations[1]	$ 16,040	$ 3,155	$ 6,599	$ 4,262	$ 2,024

(1) Represents future minimum lease payments under our leases for office and/or lab space at the following locations: 302 East Pettigrew Street, Durham, North Carolina expiring in July 2024, 3054 Cornwallis Road, Durham, North Carolina expiring in April 2026 and 20 TW Alexander Drive, Research Triangle Park, North Carolina expiring in August 2027. The lease obligations amounts above also represent future minimum lease payments on the MCAT Expansion Space as we are contractually obligated to make such payments on the MCAT Expansion Space notwithstanding that the lease commencement date for accounting purposes was not reached as of December 31, 2020 (see Note 7 to our consolidated financial statements included elsewhere in this Annual Report on Form 10-K for additional information on these lease agreements).

(2) We have entered into a license agreement with an undisclosed licensee for intellectual property used in our research programs. The agreement requires us to pay annual license fees and milestones payments for achievement of specified clinical and commercial events. We have excluded these potential milestone payments in the contractual obligations table because the timing and likelihood of these contingent payments are not currently known and would be difficult to predict or estimate.

(3) This table does not reflect principal and interest payments payable pursuant to our Pacific Western Loan Agreement, pursuant to which we may request advances on the Revolving Line of up to an aggregate principal of $30.0 million. As of December 31, 2020, we had no borrowings under our Revolving Line and, as of the date of this Annual Report on Form 10-K, the maturity date of the Revolving Line is June 23, 2023. The Revolving Line bears interest at a variable annual rate equal to the greater of (a) 2.75% above the Prime Rate (as defined in the Original Agreement), and (b) 6.00%. If the Revolving Line is terminated prior to the maturity date, we are required to pay an early termination fee equal to $0.6 million. Upon maturity or termination of the revolving line, then we are required to pay an amount equal to 1% of the maximum principal amount of the advances outstanding at any time.

In addition, we have entered into the Duke License, under which we are obligated to make aggregate future milestone payments of up to $0.2 million upon the achievement of specified corporate milestones as well as low-single digit percent royalty payments based on future net sales of applicable products and specified royalties based on sublicensing revenue. See "Business—License and Collaboration Agreements" for more information regarding our payment obligations under the Duke License. We have not included future payments under the Duke License in the table above since the payment obligations under the Duke License are contingent upon future events, such as the achievement of specified milestones or generating product sales, and we are unable to estimate the timing or likelihood of achieving these milestones or generating future product sales. We have also not included our contractual payment obligations under the Duke License in connection with the upfront payment under the Development and License Agreement with Lilly in the table above since, as of December 31, 2020, the completion of the transactions contemplated by the Development and License Agreement had not closed. We closed the transactions under the Development and License Agreement on January 6, 2021 following receipt of clearance under the Hart-Scott-Rodino Antitrust Improvements Act of 1976, as amended, and as a result we will be required to make payments under the Duke License of $3.0 million in 2021, net of any outstanding credits. See Note 14 to our audited consolidated financial statements included elsewhere in this Annual Report on Form 10-K for additional information regarding the Development and License Agreement.

We also enter into contracts in the normal course of business with CROs, CMOs, universities and other third parties for preclinical research studies, clinical trials and testing and manufacturing services. These contracts do not contain minimum purchase commitments and are cancelable by us upon prior written notice. Payments due upon cancellation consist only of payments for services provided or expenses incurred, including non-cancelable obligations of our service providers, up to the date of cancellation. These payments are not included in the table above as the amount and timing of such payments are not known.

Critical Accounting Policies and Use of Estimates

Our management's discussion and analysis of financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States ("GAAP"). The preparation of our consolidated financial statements and related disclosures requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities, costs and expenses and the disclosure of contingent assets and liabilities in our consolidated financial statements. We base our estimates on historical experience, known trends and events and various other factors

that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. We evaluate our estimates and assumptions on an ongoing basis. Our actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are described in more detail in the notes to our consolidated financial statements included elsewhere in this Annual Report on Form 10-K, 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.

Revenue Recognition

Our revenues are generated primarily through collaborative research, license, development and commercialization agreements. The terms of these agreements generally contain multiple elements, or deliverables, which may include (1) licenses, or options to obtain licenses, to use our technology, (2) research and development activities to be performed on behalf of the collaborative partner, and (3) in certain cases, services in connection with the manufacturing of preclinical and clinical material. Payments we receive under these arrangements typically include one or more of the following: non-refundable, upfront license fees; option exercise fees; funding of research and/or development efforts; clinical and development, regulatory, and sales milestone payments; and royalties on future product sales. We classify payments received under these agreements as revenues within our consolidated statements of operations.

We adopted Accounting Standards Update, or ASU, No. 2014-09, *Revenue from Contracts with Customers*, or ASC 606, on January 1, 2019 using the modified retrospective transition method. Under this method, results for reporting periods beginning on January 1, 2019 are presented under ASC 606, while prior period amounts are not adjusted and continue to be reported in accordance with ASC Topic 605, *Revenue Recognition* ("ASC 605"). ASC 606 applies to all contracts with customers, except for contracts that are within the scope of other standards. Under ASC 606, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration which the entity expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that an entity determines are within the scope of ASC 606, the entity performs 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) the entity satisfies a performance obligation.

At contract inception, once the contract is determined to be within the scope of ASC 606, we evaluate the performance obligations promised in the contract that are based on goods and services that will be transferred to the customer and determine whether those obligations are both (i) capable of being distinct and (ii) distinct in the context of the contract. Goods or services that meet these criteria are considered distinct performance obligations. If both these criteria are not met, the goods and services are combined into a single performance obligation. We then recognize as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied. Arrangements that include rights to additional goods or services that are exercisable at a customer's discretion are generally considered options. We assess if these options provide a material right to the customer and, if so, these options are considered performance obligations. The exercise of a material right is accounted for as a contract modification for accounting purposes.

We recognize as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) each performance obligation is satisfied at a point in time or over time, and if over time this is based on the use of an output or input method.

Invoices issued as stipulated in contracts prior to revenue recognition are recorded as deferred revenue. Amounts expected to be recognized as revenue within the 12 months following the balance sheet date are classified as deferred revenue within current liabilities in our consolidated balance sheets. Amounts not expected to be recognized as revenue within the 12 months following the balance sheet date are classified as noncurrent deferred revenue. Amounts recognized as revenue, but not yet invoiced are generally recognized as contract assets in the Other line item in our consolidated balance sheets.

Milestone Payments – If an arrangement includes development and regulatory milestone payments, we evaluate whether the milestones are considered probable of being reached and estimate the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within our control or the licensee's control, such as regulatory approvals, are generally not considered probable of being achieved until those approvals are received.

Royalties – For arrangements that include sales-based royalties, including milestone payments based on a level of sales, which are the result of a customer-vendor relationship and for which the license is deemed to be the predominant item to which the royalties relate, we 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. To date, we have not recognized any royalty revenue resulting from any of our licensing arrangements.

Significant Financing Component – In determining the transaction price, we adjust consideration for the effects of the time value of money if the timing of payments provides us with a significant benefit of financing. We do not assess whether a contract has a significant financing component if the expectation at contract inception is such that the period between payment by the licensees and the transfer of the promised goods or services to the licensees will be one year or less. We assessed each of our revenue arrangements in order to determine whether a significant financing component exists and concluded that a significant financing component does not exist in any of our arrangements.

Collaborative Arrangements – We have entered into collaboration agreements, which are within the scope of ASC 606, to discover, develop, manufacture and commercialize product candidates. The terms of these agreements typically contain multiple promises or obligations, which may include: (1) licenses, or options to obtain licenses, to use our technology, (2) research and development activities to be performed on behalf of the collaboration partner, and (3) in certain cases, services in connection with the manufacturing of preclinical and clinical material. Payments we receive under these arrangements typically include one or more of the following: non-refundable, upfront license fees; option exercise fees; funding of research and/or development efforts; clinical and development, regulatory, and sales milestone payments; and royalties on future product sales.

We analyze our collaboration arrangements to assess whether they are within the scope of ASU No. 2018-18 *Collaborative Arrangements*, or ASC 808, to determine whether such arrangements involve joint operating activities performed by parties that are both active participants in the activities and exposed to significant risks and rewards dependent on the commercial success of such activities. This assessment is performed throughout the life of the arrangement based on changes in the responsibilities of all parties in the arrangement. For collaboration arrangements within the scope of ASC 808 that contain multiple elements, we first determine which elements of the collaboration are deemed to be within the scope of ASC 808 and those that are more reflective of a vendor-customer relationship and, therefore, are within the scope of ASC 606. For elements of collaboration arrangements that are accounted for pursuant to ASC 808, an appropriate recognition method is determined and applied consistently, generally by analogy to ASC 606. For those elements of the arrangement that are accounted for pursuant to ASC 606, we apply the five-step model described above.

In February 2016, we entered into the Servier Agreement for the licensing of our ARCUS proprietary genome editing platform and the research, development, and manufacturing of product for clinical trials and commercialization of products. In September 2018, we entered into a collaboration and license agreement with Gilead, which we refer to as the Gilead Agreement, to develop genome editing tools using our ARCUS proprietary genome editing platform. Both agreements use our genome editing technology for the treatment of certain diseases. Consideration we received, or may receive, under these collaboration and license agreements include upfront nonrefundable payments, research funding payments and payments based upon the achievement of certain milestones and royalties on any resulting net product sales.

Under the guidance of ASC 606, certain judgments affect revenue recognition. Our primary performance obligations under our agreements consist of research and development services. Measuring the amount of time it takes for us to complete these services includes estimating our total effort to satisfy our performance obligations at the outset of the agreement and then comparing that amount to the actual effort expended for a given accounting period. In certain instances, significant judgment is required to estimate the timing of satisfying these obligations and timing may change due to efforts beyond our control, such as changes in the customer's direction of a particular research program or changes to the contractual terms of an agreement. Accordingly, our estimates may change in the future. Such changes to estimates will result in a change in prospective revenue recognition amounts.

Accrued Research and Development Expenses

As part of the process of preparing our consolidated financial statements, we are required to estimate our accrued research and development expenses. This process involves reviewing open contracts and purchase orders, communicating with our personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated costs incurred for the services when we have not yet been invoiced or otherwise notified of the actual costs. The majority of our service providers invoice us in arrears for services performed, on a pre-determined schedule or when contractual milestones are met; however, some require advance payments. We make estimates of our accrued expenses as of each balance sheet date in our consolidated financial statements based on facts and circumstances known to us at that time. Examples of estimated accrued research and development expenses include fees paid to the following:

- CROs and other third parties in connection with performing research and development activities, conducting preclinical studies and clinical trials on our behalf;
- Vendors in connection with preclinical development activities; and
- CMOs and other vendors in connection with product manufacturing and development and distribution of preclinical supplies.

We base our expenses related to preclinical studies on our estimates of the services received and efforts expended pursuant to quotes and contracts with CROs that conduct and manage preclinical studies and clinical trials and CMOs that manufacture product for our

research and development activities on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the expense. In accruing fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrual or amount of prepaid expense accordingly.

Share-Based Compensation

We measure stock options and other share-based awards granted to our employees, directors, consultants and advisors based on the fair value on the date of the grant and recognize compensation expense for those awards, net of actual forfeitures, over the requisite service period, which is generally the vesting period of the respective award.

We estimate the fair value of each stock option grant on the date of grant using the Black-Scholes option-pricing model, which uses as inputs the fair value of our common stock and assumptions we make for the expected volatility of our common stock, the expected term of our stock options, the risk-free interest rate for a period that approximates the expected term of our stock options and our expected dividend yield. As we have limited trading history, we estimate our expected volatility based on the historical volatility of publicly traded peer companies and expect to continue to do so until such time as we have adequate historical data regarding the volatility of our traded share price. The expected term of our options has been determined utilizing a weighted value considering actual exercise history and estimated expected term based on the midpoint of final vest date and expiration date. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the time of grant of the award for time periods approximately equal to the expected term of the award. Expected dividend yield is based on the fact that we have never paid cash dividends and do not expect to pay any cash dividends in the foreseeable future.

Recent Accounting Pronouncements

A description of recent accounting pronouncements that may potentially impact our financial position, results of operations or cash flows is disclosed in Note 1 to our audited consolidated financial statements included elsewhere in this Annual Report on Form 10-K.

Off-Balance Sheet Arrangements

We did not have during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined under SEC rules.

Emerging Growth Company Status

We are an "emerging growth company," as defined in the JOBS Act, and we may take advantage of reduced reporting requirements that are otherwise applicable to public companies. Section 107 of the JOBS Act exempts emerging growth companies from being required to comply with new or revised financial accounting standards until private companies are required to comply with those standards. We have elected to take advantage of the extended transition period for complying with new or revised accounting standards. As an "emerging growth company," we are also exempted from having to provide an auditor attestation of internal control over financial reporting under Sarbanes-Oxley Act Section 404(b).

We will remain an "emerging growth company" until the earliest of (1) the last day of the fiscal year in which we have total annual gross revenues of $1.07 billion or more, (2) December 31, 2024, (3) the date on which we have issued more than $1.0 billion in nonconvertible debt during the previous three years or (4) the date on which we are deemed to be a large accelerated filer under the rules of the SEC, which means the market value of our common stock held by non-affiliates exceeds $700 million as of the prior June 30th, we have been a public company for at least 12 months and have filed one Annual Report on Form 10-K.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk.

We are exposed to market risks in the ordinary course of our business. These risks primarily include interest rate sensitivities. Our interest-earning assets consist of cash and cash equivalents, which are denominated in U.S. dollars. We had cash and cash equivalents of $89.8 million, or 60% of our total assets, at December 31, 2020 and $180.9 million, or 77% of our total assets, at December 31, 2019. Interest income earned on these assets was $0.8 million and $4.3 million for the years ended December 31, 2020 and December 31, 2019, respectively. Our interest income is sensitive to changes in the general level of interest rates, primarily U.S. interest rates, however, we do not anticipate fluctuations in interest rates to have a significant impact on our financial statements.

We are also exposed to foreign exchange rate risk with respect to our global subsidiaries from foreign currency transactions. We do not anticipate foreign exchange rate risk to have a material impact on our financial statements.

Item 8. Financial Statements and Supplementary Data.

The financial statements required to be filed pursuant to this Item 8 are appended to this report and are incorporated herein by reference. An index of those financial statements is found in Item 15 of Part IV of this Annual Report on Form 10-K.

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure.

None.

Item 9A. Controls and Procedures.

Limitations on Effectiveness of Controls and Procedures

In designing and evaluating our disclosure controls and procedures, management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives. In addition, the design of disclosure controls and procedures must reflect the fact that there are resource constraints and that management is required to apply judgment in evaluating the benefits of possible controls and procedures relative to their costs.

Evaluation of disclosure controls and procedures

Our management, with the participation of our Chief Executive Officer and Interim Chief Financial Officer, evaluated, as of the end of the period covered by this Annual Report on Form 10-K, the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act). Based on that evaluation, our Chief Executive Officer and Interim Chief Financial Officer concluded that our disclosure controls and procedures were effective at the reasonable assurance level as of December 31, 2020.

Management's annual report on internal control over financial reporting

Our management, with the participation of our principal executive officer and our principal financial officer, is responsible for establishing and maintaining adequate internal control over financial reporting as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act. Our management conducted an assessment of the effectiveness of our internal control over financial reporting based on the criteria set forth in "Internal Control–Integrated Framework (2013)" issued by the Committee of Sponsoring Organizations of the Treadway Commission. Based on this assessment, management concluded that, as of December 31, 2020, our internal control over financial reporting was effective.

Attestation Report of the Registered Public Accounting Firm

Our independent registered accounting firm will not be required to opine on the effectiveness of our internal control over financial reporting pursuant to Section 404 of Sarbanes-Oxley Act of 2002 until we are no longer an "emerging growth company" as defined in the JOBS Act.

Changes in internal control over financial reporting

There were no changes in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) during the quarter ended December 31, 2020 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information.

None.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

The information required by this item will be included in our definitive proxy statement (or the "2021 Proxy Statement") to be filed with the SEC within 120 days of the end of our fiscal year covered by this Annual Report on Form 10-K and is incorporated herein by reference.

Item 11. Executive Compensation.

The information required by this item will be included in our 2021 Proxy Statement to be filed with the SEC within 120 days of the end of our fiscal year covered by this Annual Report on Form 10-K and is incorporated herein by reference.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters.

The information required by this item will be included in our 2021 Proxy Statement to be filed with the SEC within 120 days of the end of our fiscal year covered by this Annual Report on Form 10-K and is incorporated herein by reference.

Item 13. Certain Relationships and Related Transactions, and Director Independence.

The information required by this item will be included in our 2021 Proxy Statement to be filed with the SEC within 120 days of the end of our fiscal year covered by this Annual Report on Form 10-K and is incorporated herein by reference.

Item 14. Principal Accountant Fees and Services.

The information required by this item will be included in our 2021 Proxy Statement to be filed with the SEC within 120 days of the end of our fiscal year covered by this Annual Report on Form 10-K and is incorporated herein by reference.

PART IV

Item 15. Exhibits, Financial Statement Schedules.

(a)(1) Financial Statements

The following documents are included on pages F-1 through F-24 attached hereto and are filed as part of this Annual Report on Form 10-K.

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm	F-1
Consolidated Balance Sheets as of December 31, 2020 and December 31, 2019	F-2
Consolidated Statements of Operations for the Years Ended December 31, 2020 and December 31, 2019	F-3
Consolidated Statements of Stockholders' Equity for the Years Ended December 31, 2020 and December 31, 2019	F-4
Consolidated Statements of Cash Flows for the Years Ended December 31, 2020 and December 31, 2019	F-5
Notes to Consolidated Financial Statements	F-6

(a)(2) Financial Statement Schedules

All financial statement schedules have been omitted because they are not applicable, not required or the information required is shown in the financial statements or the notes thereto.

(a)(3) Exhibits

The following is a list of exhibits filed as part of this Annual Report on Form 10-K.

Exhibit Index

Exhibit Number	Description	Form	File No.	Exhibit	Filing Date	Filed Herewith
3.1	Amended and Restated Certificate of Incorporation of Precision BioSciences, Inc.	8-K	001-38841	3.1	4/1/2019	
3.2	Amended and Restated Bylaws of Precision BioSciences, Inc.	10-Q	001-38841	3.2	11/10/2020	
4.1	Specimen Common Stock Certificate	S-1/A	333-230034	4.1	3/18/2019	
4.2	Amended and Restated Investors' Rights Agreement among Precision BioSciences, Inc. and certain of its stockholders and the holders of the 2019 Notes, dated May 25, 2018, as amended	S-1/A	333-230034	4.2	3/18/2019	
4.3	Amendment No. 2, dated February 3, 2020, to the Amended and Restated Investors' Rights Agreement among Precision BioSciences, Inc. and certain of its stockholders and the holders of the 2019 Notes, dated May 25, 2018, as amended	8-K	001-38841	10.1	2/6/2020	
4.4	Form of Indenture.	S-3	333-238857	4.3	6/1/2020	
4.5	Description of the Registrant's Securities					*
10.1††	Loan and Security Agreement, dated May 15, 2019, among Precision BioSciences, Inc., Elo Life Systems, Inc. and Pacific Western Bank, as amended					*
10.2†	Development and Commercial License Agreement by and between Les Laboratoires Servier and Precision BioSciences, Inc., dated February 24, 2016, as amended	S-1	333-230034	10.1	3/1/2019	
10.3††	Amendment No. 5, dated September 18, 2019, to Development and Commercial License Agreement by and between Les Laboratoires Servier and Precision BioSciences, Inc., dated February 24, 2016, as amended	10-Q	001-38841	10.2	11/12/2019	
10.4††	Amendment No. 6, dated October 16, 2020, to Development and Commercial License Agreement by and between Les Laboratoires Servier, Institut de Recherches Internationales Servier and Precision BioSciences, Inc., dated February 24, 2016, as amended	10-Q	001-38841	10.2	11/10/2020	
10.5††	Development and License Agreement between Eli Lilly and Company and Precision BioSciences, Inc., dated November 19, 2020					*
10.6	Stock Purchase Agreement between Eli Lilly and Company and Precision BioSciences, Inc., dated November 19, 2020					*
10.7†	License Agreement by and between Duke University and Precision BioSciences, Inc., dated April 17, 2006, as amended	S-1	333-230034	10.2	3/1/2019	
10.8†	Patent Cross-License Agreement by and between Cellectis SA and Precision BioSciences, Inc., dated January 23, 2014	S-1	333-230034	10.3	3/1/2019	
10.9	Lease Agreement between Precision BioSciences, Inc. and Venable Tenant, LLC, dated April 5, 2010, as amended					*
10.10	Lease Agreement between Elo Life Systems, Inc. and ARE-NC Region No. 17, LLC, dated March 29, 2018, as amended	S-1	333-230034	10.6	3/1/2019	
10.11	Lease Agreement between Precision BioSciences, Inc. and Durham TW Alexander, LLC, dated October 2, 2018, as amended					*
10.12#	2006 Stock Incentive Plan, as amended, and form of award agreements thereunder	S-1	333-230034	10.8	3/1/2019	

Exhibit Number	Description	Form	File No.	Exhibit	Filing Date	Filed Herewith
10.13#	2015 Stock Incentive Plan, as amended, and form of award agreements thereunder	S-1	333-230034	10.9	3/1/2019	
10.14#	2019 Incentive Award Plan, and forms of award agreements thereunder					*
10.15#	2019 Employee Stock Purchase Plan	S-1/A	333-230034	10.11	3/18/2019	
10.16#	Employment Agreement between Precision BioSciences, Inc. and Matthew Kane, dated February 27, 2019	S-1/A	333-230034	10.12	3/18/2019	
10.17#	Employment Agreement between Precision BioSciences, Inc. and Derek Jantz, dated February 27, 2019	S-1/A	333-230034	10.13	3/18/2019	
10.18#	Employment Agreement between Precision BioSciences, Inc. and David Thomson, dated February 27, 2019, as amended	10-K	001-38841	10.19	3/10/2020	
10.19#	Employment Agreement between Precision BioSciences, Inc. and Fayaz Khazi, dated February 27, 2019	S-1/A	333-230034	10.16	3/18/2019	
10.20#	Employment Agreement between Precision BioSciences, Inc. and Christopher Ryan Heery, dated April 1, 2019	10-K	001-38841	10.21	3/10/2020	
10.21#	Employment Agreement between Precision BioSciences, Inc. and Dario, Scimeca dated April 11, 2019	10-K	001-38841	10.22	3/10/2020	
10.22#	Form of Indemnification Agreement between Precision BioSciences, Inc. and its directors and officers	S-1A	333-230034	10.17	3/18/2019	
10.23#	Non-Employee Director Compensation Plan	S-1A	333-230034	10.18	3/18/2019	
21.1	Subsidiaries of Precision BioSciences, Inc.					*
23.1	Consent of Deloitte & Touche LLP					*
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.					*
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.					*
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.					**
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.					**
101.INS	XBRL Instance Document					*
101.SCH	XBRL Taxonomy Extension Schema Document					*
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document					*
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document					*
101.LAB	XBRL Taxonomy Extension Label Linkbase Document					*
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document					*

* Filed herewith

** Furnished herewith

† Confidential treatment of certain provisions has been granted by the SEC pursuant to Rule 406 under the Securities Act of 1933, as amended.

†† Portions of this exhibit have been omitted pursuant to Item 601(b)(10)(iv) of Regulation S-K.
# Denotes a management contract or compensation plan or arrangement

Item 16. Form 10-K Summary

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended, the Registrant has duly caused this Report to be signed on its behalf by the undersigned, thereunto duly authorized**.**

Precision BioSciences, Inc.

Date: March 18, 2021

By: /s/Matthew Kane
Matthew Kane
President, Chief Executive Officer and Director

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, this Report has been signed below by the following persons on behalf of the Registrant in the capacities and on the dates indicated.

Name	Title	Date
/s/ Matthew Kane **Matthew Kane**	President, Chief Executive Officer and Director (*principal executive officer*)	March 18, 2021
/s/ Derek Jantz **Derek Jantz, Ph.D.**	Chief Scientific Officer and Director (*principal executive officer*)	March 18, 2021
/s/ John Alexander Kelly **John Alexander Kelly**	Interim Chief Financial Officer (*principal financial officer*)	March 18, 2021
/s/ Shane Barton **Shane Barton**	Vice President and Corporate Controller (*principal accounting officer)*	March 18, 2021
/s/ Raymond Schinazi **Raymond Schinazi, Ph.D., DSc**	Director	March 18, 2021
/s/ Shalini Sharp **Shalini Sharp**	Director	March 18, 2021
/s/ Kevin Buehler **Kevin Buehler**	Director	March 18, 2021
/s/ Geno Germano **Geno Germano**	Director	March 18, 2021
/s/ Tony Yao **Tony Yao, M.D., Ph.D.**	Director	March 18, 2021

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the stockholders and the Board of Directors of Precision BioSciences, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Precision BioSciences, Inc. and subsidiaries (the "Company") as of December 31, 2020 and 2019, the related consolidated statements of operations, changes in stockholders' equity (deficit), and cash flows, for each of the two years in the period ended December 31, 2020, 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, 2020 and 2019, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2020, in conformity with accounting principles generally accepted in the United States of America.

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 Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. 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. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits, we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

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.

/s/ Deloitte & Touche LLP

Raleigh, North Carolina

March 18, 2021

We have served as the Company's auditor since 2017.

PART I. FINANCIAL INFORMATION

Item 1. Financial Statements.

PRECISION BIOSCIENCES, INC.
CONSOLIDATED BALANCE SHEETS
(In thousands, except share and per share amounts)

	December 31, 2020	December 31, 2019
Assets		
Current assets:		
Cash and cash equivalents	$ 89,798	$ 180,886
Accounts receivable	10,000	965
Prepaid expenses	5,762	9,497
Other current assets	4	2,324
Total current assets	105,564	193,672
Property, equipment, and software—net	35,090	39,571
Intangible assets—net	1,373	1,432
Right-of-use assets—net	6,410	—
Other assets	1,721	558
Total assets	$ 150,158	$ 235,233
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 792	$ 2,037
Accrued compensation	5,745	4,425
Accrued clinical and research and development expenses	3,269	2,400
Deferred revenue	30,236	16,486
Lease liabilities	1,933	—
Other current liabilities	854	1,584
Total current liabilities	42,829	26,932
Deferred revenue	53,926	65,895
Deferred rent	—	4,092
Lease liabilities	8,586	—
Other noncurrent liabilities	392	—
Total liabilities	105,733	96,919
Commitments and contingencies (Note 7)		
Stockholders' equity:		
Preferred stock, $0.0001 par value— 10,000,000 shares authorized as of December 31, 2020 and December 31, 2019; no shares issued and outstanding as of December 31, 2020 and December 31, 2019	—	—
Common stock; $0.000005 par value— 200,000,000 shares authorized, 53,503,124 shares issued and 52,692,652 shares outstanding as of December 31, 2020; 51,965,708 shares issued and 51,155,236 shares outstanding as of December 31, 2019	—	—
Additional paid-in capital	331,450	316,333
Accumulated deficit	(286,073)	(177,067)
Treasury stock	(952)	(952)
Total stockholders' equity	44,425	138,314
Total liabilities and stockholders' equity	$ 150,158	$ 235,233

See notes to consolidated financial statements

PRECISION BIOSCIENCES, INC.
CONSOLIDATED STATEMENTS OF OPERATIONS
(In thousands, except share and per share amounts)

	For the Years Ended December 31,	
	2020	2019
Revenue	$ 24,285	$ 22,238
Operating expenses		
Research and development	98,061	82,416
General and administrative	36,052	27,026
Total operating expenses	134,113	109,442
Loss from operations	(109,828)	(87,204)
Other income (expense), net:		
Change in fair value of convertible notes payable	—	(9,758)
Interest expense	—	(182)
Interest income	822	4,267
Total other income (expense), net	822	(5,673)
Net loss and net loss attributable to common stockholders	$ (109,006)	$ (92,877)
Net loss per share attributable to common stockholders-basic and diluted	$ (2.09)	$ (2.21)
Weighted average shares of common stock outstanding-basic and diluted	52,031,740	41,991,162

See notes to consolidated financial statements

PRECISION BIOSCIENCES, INC.
CONSOLIDATED STATEMENTS OF CHANGES IN STOCKHOLDERS' EQUITY (DEFICIT)
(In thousands, except share amounts)

	Series A Convertible Preferred Stock		Series B Convertible Preferred Stock		Common Stock		Additional Paid-In	Accumulated	Treasury	Total Stockholder's Equity
	Shares	Amount	Shares	Amount	Shares	Amount	Capital	Deficit	Stock	(Deficit)
Balance- January 1, 2019	25,650,000	$ 3	21,956,095	$ 2	16,717,117	$ —	$ 126,094	$ (85,187)	$ (952)	$ 39,960
Adjustment to beginning accumulated deficit from adoption of ASU 2014-09	—	—	—	—	—	—	—	997	—	997
Conversion of convertible preferred stock into common stock upon initial public offering	(25,650,000)	(3)	(21,956,095)	(2)	22,301,190	—	5	—	—	—
Issuance of common stock upon conversion of convertible notes payable	—	—	—	—	2,921,461	—	49,490	—	—	49,490
Issuance of common stock in initial public offering, net of discounts and issuance costs	—	—	—	—	9,085,000	—	130,543	—	—	130,543
Stock option exercises	—	—	—	—	940,940	—	1,261	—	—	1,261
Share-based compensation expense	—	—	—	—	—	—	8,940	—	—	8,940
Net loss	—	—	—	—	—	—	—	(92,877)	—	(92,877)
Balance- December 31, 2019	—	—	—	—	51,965,708	—	316,333	(177,067)	(952)	138,314
Stock option exercises	—	—	—	—	1,411,188	—	691	—	—	691
Issuance of common stock under employee stock purchase plan					126,228		640			640
Share-based compensation expense	—	—	—	—	—	—	13,786	—	—	13,786
Net loss	—	—	—	—	—	—	—	(109,006)	—	(109,006)
Balance- December 31, 2020	—	$ —	—	$ —	53,503,124	$ —	$ 331,450	$ (286,073)	$ (952)	$ 44,425

See notes to consolidated financial statements

PRECISION BIOSCIENCES, INC.
CONSOLIDATED STATEMENTS OF CASH FLOWS
(In thousands)

	For the Years Ended December 31,	
	2020	2019
Cash flows from operating activities:		
Net loss	$ (109,006)	$ (92,877)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	8,777	5,317
Share-based compensation	13,786	8,940
Loss on disposal of property, equipment, and software	35	22
Non-cash interest expense	—	182
Change in fair value of convertible notes payable	—	9,758
Amortization of right-of-use assets	1,036	—
Changes in operating assets and liabilities:		
Prepaid expenses	3,735	(584)
Accounts receivable	(9,035)	(441)
Other assets and other current assets	2,194	1,032
Accounts payable	(1,455)	667
Other current liabilities	2,084	4,835
Deferred revenue	1,781	(7,866)
Lease liabilities and right-of-use assets	(1,709)	—
Other noncurrent liabilities	391	—
Net cash used in operating activities	(87,386)	(71,015)
Cash flows from investing activities:		
Purchases of property, equipment and software	(5,031)	(24,666)
Net cash used in investing activities	(5,031)	(24,666)
Cash flows from financing activities:		
Proceeds from stock option exercises	689	1,261
Proceeds from employee stock purchase plan	640	—
Deferred offering costs	—	(2,622)
Issuance of convertible notes payable	—	39,550
Proceeds from IPO, net of underwriting discounts and commissions	—	135,185
Net cash provided by financing activities	1,329	173,374
Net increase (decrease) in cash and cash equivalents	(91,088)	77,693
Cash and cash equivalents—beginning of period	180,886	103,193
Cash and cash equivalents —end of period	$ 89,798	$ 180,886
Supplemental disclosures of noncash financing and investing activities:		
Common stock issued on conversion of convertible notes payable	$ —	$ 49,490
Property, equipment and software additions included in accounts payable, accrued expenses and other current liabilities	$ 665	$ 401
Deferred offering costs included in accounts payable, accrued expenses and other current liabilities	$ —	$ 168

See notes to consolidated financial statements

NOTE 1: DESCRIPTION OF BUSINESS AND SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

Description of Business

Precision BioSciences, Inc. (the "Company") was incorporated on January 26, 2006 under the laws of the State of Delaware and is based in Durham, North Carolina. The Company is dedicated to improving life through the application of its pioneering, proprietary ARCUS genome editing platform to treat human diseases and create healthy and sustainable food and agricultural solutions. The Company is actively developing product candidates through two reportable segments: Therapeutics and Food. The Therapeutics segment is focused on allogeneic CAR T cell immunotherapy and *in vivo* gene correction. The Food segment focuses on applying ARCUS to develop food and nutrition products through collaboration agreements with consumer-facing companies.

The Company's 100% owned subsidiary, Precision PlantSciences, Inc., was incorporated on January 4, 2012. Precision PlantSciences, Inc. amended its certificate of incorporation on January 16, 2018 to change its name to Elo Life Systems, Inc. Elo Life Systems Australia Pty Ltd was incorporated on May 29, 2018 as a 100% owned subsidiary of Elo Life Systems, Inc. Additionally, the Company's 100% owned subsidiary, Precision BioSciences UK Limited, was incorporated on June 17, 2019. The accompanying consolidated financial statements include the accounts of the Company and its subsidiaries. Intercompany balances and transactions have been eliminated in consolidation.

Since its inception, the Company has devoted substantially all of its efforts to research and development activities, recruiting skilled personnel, developing manufacturing processes, establishing its intellectual property portfolio and providing general and administrative support for these operations. The Company is subject to a number of risks similar to those of other companies conducting high-risk, early-stage research and development of product candidates. Principal among these risks are dependence on key individuals and intellectual property, competition from other products and companies, and the technical risks associated with the successful research, development and clinical manufacturing of its product candidates. The Company's success is dependent upon its ability to continue to raise additional capital in order to fund ongoing research and development, obtain regulatory approval of its products, successfully commercialize its products, generate revenue, meet its obligations, and, ultimately, attain profitable operations.

On April 1, 2019, the Company completed its initial public offering ("IPO") in which the Company issued and sold 9,085,000 shares of its common stock at a public offering price of $16.00 per share and received approximately $130.5 million in net proceeds, after deducting underwriting discounts and commission of approximately $10.2 million and issuance costs of approximately $4.6 million.

In connection with the IPO, on March 15, 2019 the Company effected a reverse split of shares of the Company's common stock on a 1-for-2.134686 basis (the "Reverse Stock Split") of its issued and outstanding shares of common stock and a proportional adjustment to the existing conversion ratios for the Company's Series A and Series B preferred stock. Accordingly, all common shares, stock option shares, and per share amounts for all periods presented in the accompanying financial statements and notes thereto have been retroactively adjusted, where applicable, to reflect this Reverse Stock Split and adjustment of the preferred stock conversion ratios.

Authorized common shares were not affected by the Reverse Stock Split. Upon the closing of the IPO, all of the outstanding shares of convertible preferred stock automatically converted into 22,301,190 shares of common stock at the applicable ratio then in effect and the outstanding convertible notes payable, including accrued interest, were settled into 2,921,461 shares of common stock. Subsequent to the closing of the IPO, there were no shares of Series A or Series B convertible preferred stock or convertible notes payable outstanding.

Use of Estimates

The preparation of consolidated financial statements in conformity with accounting principles generally accepted in the United States of America ("GAAP") requires management to make estimates and assumptions that affect the amounts reported in the consolidated financial statements and disclosures made in the accompanying notes to the consolidated financial statements. Actual results could differ from those estimates. Significant estimates include recording revenue for performance obligations recognized over time, determination of the fair value of share-based compensation grants and estimating services expended by third-party service providers used to recognize research and development expense.

Basis of Presentation

These financial statements have been prepared in accordance with GAAP. Additionally, the accompanying consolidated financial statements have been prepared on a going concern basis, which contemplates the realization of assets and the satisfaction of liabilities in the normal course of business. As of December 31, 2020, the Company has not generated any revenue from product sales and does not expect to generate any revenue from the sale of product in the foreseeable future. During the year ended December 31, 2020, the Company incurred a net loss of $109.0 million and, as of December 31, 2020, has an accumulated deficit of $286.1 million. The Company has financed operations primarily through upfront payments from collaboration and licensing agreements, its initial public

offering ("IPO"), and private placements of convertible preferred stock and convertible debt. The Company expects to incur additional operating losses and negative operating cash flows for the foreseeable future.

Management believes that cash and cash equivalents as of December 31, 2020, cash payments received from Lilly in January 2021 in connection with the closing of the Development and License Agreement, expected operational receipts and available credit will allow the Company to continue its operations into 2023. In the absence of a significant source of recurring revenue, the continued viability of the Company beyond that point is dependent on its ability to continue to raise additional capital to finance its operations. There can be no assurance that the Company will be able to obtain sufficient capital to cover its costs on acceptable terms, if at all.

Summary of Significant Accounting Policies

Cash and Cash Equivalents

The Company considers all highly liquid investments with an original maturity of three months or less at the date of purchase to be cash equivalents. As of December 31, 2020, the Company held an insignificant amount of cash equivalents. As of December 31, 2019, the Company held cash equivalents composed of money market funds and repurchase agreements that were purchased through repurchase intermediary banks and collateralized by deposits in the form of government securities and obligations.

Concentrations of Credit Risk

Financial instruments that potentially subject the Company to concentrations of credit risk consist principally of cash. All of the Company's cash and cash equivalents are held at financial institutions that management believes to be of high credit quality. The Company may maintain cash deposits in financial institutions in excess of government insured limits. The Company regularly invests excess cash deposits in money market funds and repurchase agreements. The Company believes that the credit risk arising from the holdings of these financial instruments is mitigated by the fact that these securities are of short duration, government backed and of high credit rating. The Company has not experienced any losses on cash and cash equivalents to date.

Revenue from two development and license agreements accounted for 16% and 74% of revenue during 2020 and 60% and 33% of revenue during 2019. One development and license agreement accounted for 98% of deferred revenue as of December 31, 2020.

Deferred Equity Offering Costs

The Company capitalizes incremental legal, professional accounting and other third-party fees directly associated with the Company's planned equity offerings as other current assets until the equity offering is consummated. After consummation, these costs are recorded in stockholders' equity (deficit) as a reduction of additional paid-in capital. If the equity offering is aborted, any costs deferred are expensed immediately.

Property, Equipment and Software

Property, equipment and software are stated at cost, net of depreciation and amortization. Depreciation and amortization are calculated using the straight-line method over the estimated useful lives of the assets ranging from three to seven years. Leasehold improvements are amortized on a straight-line basis over the shorter of the lease term or estimated useful life of the asset.

The depreciation and amortization periods for the Company's significant property, equipment and software categories are as follows:

Laboratory equipment	5 to 7 years
Furniture and fixtures and office equipment	3 to 5 years
Leasehold improvements	Lesser of remaining lease term or useful life

Repairs and maintenance are charged to operations as incurred, and expenditures for additions and improvements that extend the useful life of the asset are capitalized.

Intangible Assets

Intangible assets primarily include licenses and patents. The Company capitalizes license fees paid to acquire access to proprietary technology if the technology is expected to have alternative future use in multiple research and development projects. The cost of licensed technology rights is amortized using the straight-line method over the estimated useful life of the technology. If the access to use the technology rights is one year or less, the cost is recorded as a prepaid expense and amortized over the period identified in the agreement. Amortization expense for licensed technology and capitalized patent costs is included in research and development expenses within the accompanying consolidated statement of operations.

Impairment of Long-Lived Assets

Long-lived assets, such as property, equipment and software and intangible assets, subject to amortization, are reviewed for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable. An impairment loss is assessed when future undiscounted cash flows are less than the assets' carrying value and recognized when the carrying value of the asset exceeds fair value. Fair value is calculated by estimating the discounted future cash flows expected to be generated by the asset as well as other valuation techniques. An impairment charge is recognized for the amount by which the carrying amount exceeds the fair value of the asset.

Leases

In February 2016, the Financial Accounting Standards Board ("FASB") issued Accounting Standards Update ("ASU") 2016-02, *Leases* ("ASC 842"), to enhance the transparency and comparability of financial reporting related to leasing arrangements. The Company adopted ASC 842 on January 1, 2020, or the effective date, and used the effective date as its date of initial application.

At the inception of an arrangement, the Company determines whether the arrangement is or contains a lease based on the unique facts and circumstances present. Leases with a term greater than one year are recognized on the balance sheet as right-of-use assets and lease liabilities. The Company has elected not to recognize on the balance sheet leases with terms of one year or less. Lease liabilities and corresponding right-of-use assets are recorded based on the present value of lease payments over the expected remaining lease term. Certain adjustments to the right-of-use asset were required for items such as prepaid and deferred rent. In calculating the present value of the lease payments, the Company has elected to apply the discount rate based on the remaining lease term as of the transition date, January 1, 2020. As the rate implicit in the lease is not readily determinable, the Company utilizes its incremental borrowing rates, which are the rates incurred to borrow on a collateralized basis over a similar term an amount equal to the lease payments in a similar economic environment.

The Company has elected to account for the lease and non-lease components of each of its operating leases as a single lease component. In addition, the Company elected the package of practical expedients permitted under the transition guidance within ASC 842, in which the Company need not reassess (i) the historical lease classification, (ii) whether any expired or existing contract is or contains a lease, or (iii) the initial direct costs for any existing leases. The operating right-of-use asset recorded on the balance sheet is amortized on a straight-line basis as lease expense.

Revenue Recognition for Contracts with Customers

The Company's revenues are generated primarily through collaborative research, license, development and commercialization agreements.

Effective January 1, 2019, the Company adopted Accounting Standards Update ("ASU") No. 2014-09, *Revenue from Contracts with Customers* ("ASC 606"), using the modified retrospective transition method. The Company applied the modified retrospective transition method to contracts that were not completed as of January 1, 2019. ASC 606 applies to all contracts with customers, except for contracts that are within the scope of other standards. Under ASC 606, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration which the entity expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that an entity determines are within the scope of ASC 606, the entity performs 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) the entity satisfies a performance obligation.

At contract inception, once the contract is determined to be within the scope of ASC 606, the Company evaluates the performance obligations promised in the contract that are based on goods and services that will be transferred to the customer and determines whether those obligations are both (i) capable of being distinct and (ii) distinct in the context of the contract. Goods or services that meet these criteria are considered distinct performance obligations. If both these criteria are not met, the goods and services are

combined into a single performance obligation. The Company then recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied. Arrangements that include rights to additional goods or services that are exercisable at a customer's discretion are generally considered options. The Company assesses if these options provide a material right to the customer and if so, these options are considered performance obligations. The exercise of a material right is accounted for as a contract modification for accounting purposes.

The Company recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) each performance obligation is satisfied at a point in time or over time, and if over time this is based on the use of an output or input method. For the year ended December 31, 2020, the Company recorded cumulative catch up adjustments that reduced revenue recognition by $5.2 million, in addition to a contract liability adjustment, for changes in total estimated effort to be incurred in the future to satisfy the performance obligation and changes to the transaction price related to variable consideration for development milestones that were constrained in prior periods.

Invoices issued as stipulated in contracts prior to revenue recognition are recorded as deferred revenue. Amounts expected to be recognized as revenue within the 12 months following the balance sheet date are classified as deferred revenue within current liabilities in the accompanying consolidated balance sheets. Amounts not expected to be recognized as revenue within the 12 months following the balance sheet date are classified as noncurrent deferred revenue. Amounts recognized as revenue, but not yet invoiced are generally recognized as contract assets in the other current assets line item in the accompanying consolidated balance sheets.

Milestone Payments – If an arrangement includes development and regulatory milestone payments, the Company evaluates whether the milestones are considered probable of being reached and estimates the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within the Company's or the licensee's control, such as regulatory approvals, are not considered probable of being achieved until those approvals are received and therefore revenue recognized is constrained as management is unable to assert that a reversal of revenue would not be probable. The transaction price is then allocated to each performance obligation on a relative standalone selling price basis, for which the Company recognizes revenue as or when the performance obligations under the contract are satisfied. At the end of each subsequent reporting period, the Company re-evaluates the probability of achievement of such development milestones and any related constraint, and, if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect collaboration revenues and earnings in the period of adjustment.

Royalties – For arrangements that include sales-based royalties, including milestone payments based on a level of sales, which are the result of a customer-vendor relationship and for which the license is deemed to be the predominant item to which the royalties relate, the Company recognizes revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation linked to some or all of the royalty has been satisfied or partially satisfied. To date, the Company has not recognized any royalty revenue resulting from any of its licensing arrangements.

Significant Financing Component – In determining the transaction price, the Company adjusts consideration for the effects of the time value of money if the timing of payments provides the Company with a significant benefit of financing. The Company does not assess whether a contract has a significant financing component if the expectation at contract inception is such that the period between payment by the licensees and the transfer of the promised goods or services to the licensees will be one year or less. The Company assessed each of its revenue arrangements in order to determine whether a significant financing component exists and concluded that a significant financing component does not exist in any of its arrangements.

Collaborative Arrangements – The Company has entered into collaboration agreements, which are within the scope of ASC 606, to discover, develop, manufacture and commercialize product candidates. The terms of these agreements typically contain multiple promises or obligations, which may include: (1) licenses, or options to obtain licenses, to use the Company's technology, (2) research and development activities to be performed on behalf of the collaboration partner, and (3) in certain cases, services in connection with the manufacturing of preclinical and clinical material. Payments the Company receives under these arrangements typically include one or more of the following: non-refundable, upfront license fees; option exercise fees; funding of research and/or development efforts; clinical and development, regulatory, and sales milestone payments; and royalties on future product sales.

The Company analyzes its collaboration arrangements to assess whether the collaboration agreements are within the scope of accounting standards codification ("ASC") ASC 808, *Collaborative Arrangements* ("ASC 808") to determine whether such arrangements involve joint operating activities performed by parties that are both active participants in the activities and exposed to significant risks and rewards dependent on the commercial success of such activities. This assessment is performed throughout the life of the arrangement based on changes in the responsibilities of all parties in the arrangement. For collaboration arrangements within the scope of ASC 808 that contain multiple elements, the Company first determines which elements of the collaboration are deemed to be within the scope of ASC 808 and those that are more reflective of a vendor-customer relationship and, therefore, are within the scope

of ASC 606. For elements of collaboration arrangements that are accounted for pursuant to ASC 808, an appropriate recognition method is determined and applied consistently, generally by analogy to ASC 606. For those elements of the arrangement that are accounted for pursuant to ASC 606, the Company applies the five-step model described above.

For additional discussion of accounting for collaboration revenues, see Note 12, "Collaboration and license agreements."

Research and Development

Research and development costs are expensed as incurred. Research and development expenses are comprised of costs incurred in performing research and development activities including salaries, benefits, share-based compensation, allocations for rent and facility costs, depreciation, preclinical manufacturing expenses, costs of services provided by contract research organizations ("CROs") in connection with preclinical trials and contract manufacturing organizations ("CMOs") engaged to manufacture clinical trial material, costs of licensing technology, and costs of services provided by research organizations and service providers. Upfront payments and milestone payments made for the licensing of technology are expensed as research and development in the period in which they are incurred if the technology is not expected to have any alternative future uses other than the specific research and development project for which it was intended. Nonrefundable advance payments for goods or services to be received in the future for use in research and development activities are recorded as prepaid expenses. The prepaid amounts are expensed as the related goods are delivered or the services are performed rather than when the payment is made.

The Company is required to estimate accrued research and development expenses resulting from its obligations under contracts with CROs, CMOs, research organizations, service providers, vendors and consultants in connection with research and development activities. The financial terms of these contracts are subject to negotiations and vary from contract to contract and may result in payment flows that do not match the periods over which materials or services are provided to the Company under such contracts. The Company's objective is to reflect the appropriate research and development expenses in its consolidated financial statements by matching those expenses with the period in which the services and efforts are expended. There may be instances in which payments made to the Company's vendors will exceed the level of services provided and result in a prepayment of the expense. In accruing fees, the Company estimates the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from the Company's estimate, the Company adjusts the accrual or amount of prepaid expense accordingly.

Comprehensive Loss

Comprehensive loss includes net loss as well as other changes in stockholders' equity (deficit) that result from transactions and economic events other than those with stockholders. For the years ended December 31, 2020 and December 31, 2019, there was no difference between net loss and comprehensive loss in the accompanying consolidated financial statements.

Net Loss Per Share

Basic net loss per share is computed by dividing net loss attributable to common stockholders by the weighted-average number of shares of common stock outstanding during the period. Diluted net loss per share is computed using the weighted-average number of shares of common stock outstanding during the period and, if dilutive, the weighted-average number of potential shares of common stock. Diluted net loss per share is the same as basic net loss per share for the years ended December 31, 2020 and December 31, 2019 given all potential shares of common stock are anti-dilutive as a result of the net loss.

Share-Based Compensation

The Company accounts for all share-based compensation, including stock options and the employee stock purchase plan at fair value and recognizes compensation expense for those equity awards, net of actual forfeitures, over the requisite service period, which is generally the vesting period of the respective award.

The fair value of each equity grant is estimated on the date of grant using the Black-Scholes option-pricing model, which uses as inputs the fair value of the Company's common stock and assumptions the Company makes for the expected volatility of its common stock, the expected term of the stock options, the risk-free interest rate for a period that approximates the expected term of the stock options and the Company's expected dividend yield. As the Company has limited trading history, expected volatility is estimated based on the historical volatility of publicly traded peer companies and the Company expects to continue to do so until such time as it has adequate historical data regarding the volatility of its traded share price. The expected term of the options has been determined utilizing a weighted value considering actual exercise history and estimated expected term based on the midpoint of final vest date and expiration date. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the time of grant of the award for time periods approximately equal to the expected term of the award. Expected dividend yield is based on the fact that the Company has never paid cash dividends and does not expect to pay any cash dividends in the foreseeable future.

Income Taxes

Deferred tax assets and liabilities are determined based on the temporary differences between the consolidated financial statement carrying amounts and the tax basis of assets and liabilities using the enacted tax rates in effect in the years in which the differences are expected to reverse. In estimating future tax consequences, all expected future events are considered other than the enactment of changes in the tax law or rates. Changes in deferred tax assets and liabilities are recorded in the provision for income taxes.

The Company may recognize the tax benefit from an uncertain tax position only if it is more likely than not that the tax position will be sustained on examination by the taxing authorities based on the technical merits of the position. The tax benefits recognized in the consolidated financial statements from such a position is measured based on the largest benefit that has a greater than 50% likelihood of being realized upon ultimate settlement.

The Company assesses the likelihood that its deferred tax assets will be recovered from future taxable income and, to the extent it believes, based upon the weight of available evidence, that it is more likely than not that all or a portion of the deferred tax assets will not be realized, a valuation allowance is established through a charge to income tax expense. Potential for recovery of deferred tax assets is evaluated by estimating the future taxable profits expected and considering prudent and feasible tax planning strategies.

Accounting Standards Updates

The Company is an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, and may take advantage of reduced reporting requirements that are otherwise applicable to public companies. Section 107 of the JOBS Act exempts emerging growth companies from being required to comply with new or revised financial accounting standards until private companies are required to comply with those standards. The Company has elected to use the extended transition period for complying with new or revised accounting standards. The JOBS Act also exempts the Company from having to provide an auditor attestation of internal controls over financial reporting under Sarbanes-Oxley Act Section 404(b).

The Company will remain an "emerging growth company" until the earliest of (i) December 31, 2024, (ii) the last day of the fiscal year in which it has total annual gross revenues of $1.07 billion or more, (iii) the date on which it has issued more than $1.0 billion in nonconvertible debt during the previous three years or (iv) the date on which it is deemed to be a large accelerated filer under the rules of the Securities and Exchange Commission ("SEC"), which generally is when it has more than $700 million in market value of its stock held by non-affiliates as of the prior June 30th.

In February 2016, the FASB issued ASU 2016-02, Leases ("ASC 842"). This standard was issued in order to improve comparability among organizations by recognizing lease assets and liabilities for all leases, with certain exceptions, on the balance sheet. The Company elected to early adopt ASC 842 on January 1, 2020, or the effective date, and used the effective date as its date of initial application. As such, the Company did not adjust prior period amounts. The Company also elected to utilize various practical expedients upon transition, which permits companies to not reassess lease identification, classification, and initial direct costs under ASC 842 for leases that commenced prior to the effective date. Upon adoption, the Company recorded lease liabilities of $11.6 million, right-of-use assets of $6.8 million, and a reduction of existing deferred rent balances of $4.8 million on the balance sheet as of January 1, 2020.

In May 2014, the FASB, issued ASC 606, which superseded the revenue requirements in ASC 605. In 2015 and 2016, the FASB issued additional ASUs related to ASC 606 that delayed the effective date of the guidance and clarified various aspects of the new revenue guidance, including principal versus agent considerations, identifying performance obligations, and licensing, and they include other improvements and practical expedients. Effective January 1, 2019, the Company adopted ASC 606 using the modified retrospective transition method.

As a result of adopting ASC 606, the Company recorded a $1.0 million transition adjustment in the first quarter of 2019 to reduce the opening balance of accumulated deficit as of January 1, 2019 primarily as a result of the treatment of the up-front consideration received from the Company's collaboration agreements under prior revenue recognition guidance. During the year ended December 31, 2020, the Company recorded $19.5 million in revenue that was included in deferred revenue as of December 31, 2019.

Other accounting standards updates issued, but not effective until after December 31, 2020, are not expected to have a material effect on the Company's consolidated financial position, statements of operations or cash flows.

NOTE 2: PROPERTY, EQUIPMENT AND SOFTWARE

Property, equipment and software consisted of the following as of December 31 (in thousands):

	2020	2019
Construction in progress	$ 1,894	$ 697
Leasehold improvements	26,580	25,969
Software	394	328
Laboratory equipment	21,240	19,251
Office equipment	1,542	1,602
Furniture and fixtures	2,518	2,373
Total property, equipment and software	54,168	50,220
Less accumulated depreciation and amortization	19,078	10,649
Property, equipment and software - net	$ 35,090	$ 39,571

Depreciation expense, including amortization of leasehold improvements and software, was $8.7 million and $5.3 million for the years ended December 31, 2020 and December 31, 2019, respectively.

NOTE 3: INTANGIBLE ASSETS

Intangible assets, net, consisted of the following as of December 31 (in thousands):

	2020	2019
License cost	$ 1,831	$ 1,831
Less: accumulated amortization	(340)	(281)
Less: impairments	(118)	(118)
Intangible assets, net	1,373	1,432

Amortization expense of intangible assets was less than $0.1 million for the years ended December 31, 2020 and December 31, 2019. Amortization expense for intangible assets with definite lives will be less than $0.1 million for each of the next five years with the remaining $0.7 million amortized to expense in 2026 and beyond.

NOTE 4: STOCKHOLDERS' EQUITY

Capital Structure

Upon the closing of the IPO, all of the Company's outstanding shares of the Series A and Series B convertible preferred stock automatically converted into 22,301,190 shares of common stock and the Company's outstanding convertible notes payable, including accrued interest, converted into 2,921,461 shares of common stock at the applicable conversion ratio. Subsequent to the closing of the IPO, there were no shares of preferred stock outstanding.

On April 1, 2019, the Company filed an amendment to its amended and restated certificate of incorporation pursuant to which, among other things, the Company increased its authorized shares to 210,000,000 shares of capital stock, of which 200,000,000 shares were designated as $0.000005 par value common stock and 10,000,000 shares were designated as $0.0001 par value preferred stock.

NOTE 5: SHARE-BASED COMPENSATION

The Company previously granted stock options under its 2006 Stock Incentive Plan (the "2006 Plan") and its 2015 Stock Incentive Plan (the "2015 Plan"). As of December 31, 2020 there were 5,031,848 stock options outstanding under the 2006 Plan and 2015 Plan and no remaining stock options available to be granted under such plans.

On March 12, 2019, the Company's board of directors adopted, and, on March 14, 2019 the Company's stockholders approved, the Precision BioSciences, Inc. 2019 Incentive Award Plan ("2019 Plan") and the 2019 Employee Stock Purchase Plan ("2019 ESPP"), both of which became effective on March 27, 2019.

The 2019 Plan provides for the grant of incentive stock options, non-qualified stock options, stock appreciation rights, restricted stock, restricted stock units and other share-based awards. The number of shares available for issuance under the 2019 Plan initially equaled 4,750,000 shares of common stock. The 2019 Plan provides for an annual increase to the number of shares of common stock available for issuance on the first day of each calendar year beginning January 1, 2020 and ending on and including January 1, 2029 by an amount equal to the lesser of (i) 4% of the aggregate number of shares of common stock outstanding on the final day of the immediately preceding calendar year and (ii) such smaller number of shares of common stock as determined by the board of directors. As of January 1, 2021, the aggregate number of shares available for issuance under the 2019 Plan has been increased by 4,153,915 pursuant to this provision. Any shares that are subject to awards outstanding under the Company's 2006 Plan and 2015 Plan as of the effective date of the 2019 Plan that expire, lapse, or are terminated, exchanged for cash, surrendered, repurchased, or canceled without having been fully exercised or forfeited, to the extent so unused, will become available for award grants under the 2019 Plan. As of December 31, 2020, 1,933,781 shares were available to be issued under the 2019 Plan. The 2019 Plan had 5,512,422 stock options outstanding as of December 31, 2020.

Up to 525,000 shares of the Company's common stock were initially reserved for issuance under the 2019 ESPP. The 2019 ESPP provides for an annual increase to the number of shares available for issuance on the first day of each calendar year beginning January 1, 2020 and ending on and including January 1, 2029 by an amount equal to the lesser of (i) 1% of the shares outstanding on the final day of the immediately preceding calendar year and (ii) such smaller number of shares as is determined by our board of directors. As of January 1, 2021, the aggregate number of shares available for issuance under the 2019 ESPP has been increased by 1,038,478 shares pursuant to this provision. No more than 5,250,000 shares of our common stock may be issued under our 2019 ESPP. The purchase price of the shares under the 2019 ESPP, in the absence of a contrary designation, will be 85% of the lower of the fair market value of our common stock on the first trading day of the offering period or on the purchase date. As of December 31, 2020, we had issued 126,228 shares under the 2019 ESPP. As of December 31, 2020, 910,324 shares were available to be issued under the 2019 ESPP. The Company recognized share-based compensation expense related to the ESPP of $0.4 million and less than $0.1 million during the years ended December 31, 2020 and December 31, 2019, respectively.

The Company recorded employee and nonemployee share-based compensation expense as follows (in thousands):

	Years Ended December 31,	
	2020	2019
Employee	$ 12,639	$ 8,354
Nonemployee	1,147	586
	$ 13,786	$ 8,940

Share-based compensation expense is included in the following line items in the consolidated statements of operations (in thousands):

	Years Ended December 31,	
	2020	2019
Research and development	$ 8,338	$ 5,639
General and administrative	5,448	3,301
	$ 13,786	$ 8,940

Determining the appropriate fair value model to measure the fair value of the stock option grants on the date of grant and the related assumptions requires judgment. The fair value of each stock option grant is estimated using a Black-Scholes option-pricing model on the date of grant as follows:

	Years Ended December 31,	
	2020	2019
Estimated dividend yield	0.00%	0.00%
Weighted-average expected stock price volatility	73.70%	68.25%
Weighted-average risk-free interest rate	0.60%	1.98%
Expected term of options (in years)	6.55	6.61
Weighted-average fair value per option	$ 4.81	$ 7.62

The expected volatility rates are estimated based on the actual volatility of comparable public companies over the expected term. The expected term represents the average time that stock options that vest are expected to be outstanding. The Company does not have sufficient history of exercising stock options to estimate the expected term of employee stock options and thus utilizes a weighted value considering actual history and estimated expected term based on the midpoint of final vest date and expiration date. The risk-free rate is based on the United States Treasury yield curve during the expected life of the option.

The following table summarizes activity in the Company's stock option plans for the years ended December 31, 2020 and December 31, 2019:

	Outstanding Option Shares	Weighted-Average Exercise Price
Balance as of January 1, 2019	7,763,464	5.00
Granted	2,647,236	11.64
Exercised	(940,940)	1.34
Forfeited/canceled	(550,644)	10.47
Balance as of December 31, 2019	8,919,116	7.02
Granted	4,011,728	7.26
Exercised	(1,411,188)	0.49
Forfeited/canceled	(975,386)	8.17
Balance as of December 31, 2020	10,544,270	7.88

The intrinsic value of stock options exercised was $10.3 million and $10.6 million during the years ended December 31, 2020 and December 31, 2019, respectively.

There was approximately $30.5 million of total unrecognized compensation cost related to unvested stock options as of December 31, 2020, which is expected to be recognized over a weighted-average period of 2.5 years.

The following table summarizes certain information about stock options granted under the stock option plans which are vested or expected to vest as of December 31, 2020 and December 31, 2019.

Years Ended December 31,		Number of Options	Weighted-Average Remaining Contractual Life (in years)		Weighted-Average Exercise Price
2020	Expected to be exercisable	10,544,270	7.23	$	7.88
2020	Currently exercisable	4,582,708	5.48	$	6.69
2019	Expected to be exercisable	8,919,116	7.19	$	7.02
2019	Currently exercisable	4,082,663	5.08	$	3.12

The following table summarizes certain information about stock options outstanding under the stock option plans for the years ending December 31, 2020 and December 31, 2019, respectively:

Year Ended December 31, 2020			
Exercise price	Number of Options Outstanding	Weighted- Average Remaining Life	Number of Options Exercisable
$0.01 - $0.04	717,949	0.61	717,949
$0.41 - $1.20	1,472,717	5.11	1,364,991
$5.67 - $9.46	4,414,103	8.75	494,811
$10.17 - $13.80	3,874,957	7.58	1,954,663
$14.91 - $16.00	64,544	4.51	50,294
	10,544,270		4,582,708

Year Ended December 31, 2019			
Exercise price	Number of Options Outstanding	Weighted- Average Remaining Life	Number of Options Exercisable
$0.01 - $0.04	1,385,203	1.50	1,385,203
$0.41 - $1.20	2,310,993	6.32	1,721,811
$7.74 - $9.46	1,266,454	9.44	131,644
$10.17 - $13.80	3,891,922	8.96	844,005
$14.91 - $16.00	64,544	9.59	—
	8,919,116		4,082,663

NOTE 6: RETIREMENT PLAN

In January 2011, the Company established a defined contribution 401(k) retirement savings plan (the "Retirement Plan") to all full-time employees. Employee contributions to the Retirement Plan can be 100% of annual compensation up to the prescribed annual maximum under the Internal Revenue Code. Administrative fees of less than $0.1 million were paid by the Company for the years ended December 31, 2020 and December 31, 2019.

The Retirement Plan includes a safe-harbor matching employer contribution equal to 100% of participants' deferral contributions up to 4%. The Company made contributions of $0.8 million and $0.6 million to the Retirement Plan during the years ended December 31, 2020 and December 31, 2019, respectively. Retirement plan contributions made by the Company are recorded to research and development expense and general and administrative expense as incurred and are included in the consolidated statement of operations.

NOTE 7: COMMITMENTS AND CONTINGENCIES

Litigation

The Company is subject to various legal matters and claims in the ordinary course of business. Although the results of legal proceedings and claims cannot be predicted with certainty, in the opinion of management, there are currently no such known matters that will have a material effect on the consolidated financial condition, results of operations or cash flows of the Company.

COVID-19 Pandemic

In March 2020, the World Health Organization designated the outbreak of the novel strain of coronavirus known as COVID-19 as a global pandemic. The Company has taken steps in line with guidance from the U.S. Centers for Disease Control and Prevention ("CDC") and the State of North Carolina to protect the health and safety of its employees and the community.

The Company is working closely with its clinical sites, physician partners and the patient community to monitor and manage the ongoing impact of the COVID-19 pandemic. The Company remains committed to its clinical programs and development plans, however, disruptions, competing resource demands and safety concerns caused by the COVID-19 pandemic have caused delays in the Company's clinical trial site activation and impacted its ability to enroll patients. The Company may also experience other difficulties, disruptions or delays in conducting preclinical studies or initiating, enrolling, conducting or completing its planned and ongoing clinical trials, and the Company may incur other unforeseen costs as a result. While the extent to which COVID-19 may continue to impact the Company's future results will depend on future developments, the pandemic and associated economic impacts could result in a material impact to the Company's future financial condition, results of operations and cash flows. The Company is continuing to assess the impact of the COVID-19 pandemic to best mitigate risk and continue the operations of its business.

Leases

The Company has operating leases for real estate in North Carolina and does not have any finance leases.

Many of the Company's leases contain options to renew and extend lease terms and options to terminate leases early. Reflected in the right-of-use asset and lease liabilities on the Company's consolidated balance sheet are the periods provided by renewal and extension options that the Company is reasonably certain to exercise, as well as the periods provided by termination options that the Company is reasonably certain to not exercise.

The Company has existing leases that include variable lease payments that are not included in the right-of-use asset and lease liabilities and are reflected as an expense in the period incurred. Such payments primarily include common area maintenance charges and fluctuations in rent payments that are driven by factors such as future changes in an index (e.g. the Consumer Price Index).

The Company has existing leases in which the non-lease components (e.g., common area maintenance, consumables, etc.) are paid separately from rent based on actual costs incurred and therefore are not included in the right-of-use assets and lease liabilities but rather reflected as an expense in the period incurred. The elements of lease expense were as follows:

(in thousands)	Year Ended December 31, 2020
Lease Cost	
Operating lease cost	$ 1,922
Short-term lease cost	405
Variable lease cost	926
Total Lease Cost	$ 3,253
Other Information	
Operating cash flows used for operating leases	2,755
Operating lease liabilities arising from obtaining right-of-use assets	623
Operating Leases	
Weighted average remaining lease term (in years)	4.7
Operating Leases	
Weighted average discount rate	7.9%

Future lease payments under non-cancelable leases with terms of greater than one year as of December 31, 2020, were as follows:

(in thousands)	December 31, 2020
2021	$ 2,685
2022	2,769
2023	2,848
2024	2,134
2025	1,086
2026 and beyond	1,108
Total lease payments	12,630
Less: imputed interest	2,111
Total operating lease liabilities	$ 10,519

Supply Agreements

The Company enters into contracts in the normal course of business with CMOs for the manufacture of clinical trial materials and CROs for clinical trial services. These agreements provide for termination at the request of either party with less than one-year notice and are, therefore, cancelable contracts and, if canceled, are not anticipated to have a material effect on the consolidated financial condition, results of operations, or cash flows of the Company.

NOTE 8: NET LOSS PER SHARE

The Company's potential dilutive securities have been excluded from the computation of diluted net loss per share as the effect would be to reduce the net loss per share. Therefore, the weighted-average number of shares of common stock outstanding used to calculate both basic and diluted net loss per share attributable to common stockholders is the same.

The Company excluded the following potential shares of common stock from the computation of diluted net loss per share attributable to common stockholders because including them would have had an anti-dilutive effect:

	Years Ended December 31,	
	2020	2019
Outstanding share-based compensation awards	10,544,270	4,032,359
Total	10,544,270	4,032,359

NOTE 9: DEBT

In March 2019, the Company entered into a note purchase agreement pursuant to which it sold and issued an aggregate of $39.6 million of convertible notes payable (the "2019 Notes").

The 2019 Notes accrued interest at a rate of 6% per annum. The 2019 Notes were settled in 2,921,461 shares of common stock in connection with the closing of the Company's IPO (see Note 1) at a settlement price of $13.60 per share (equal to 85% of the IPO price per share).

On issuance, the Company elected to account for the 2019 Notes at fair value with any changes in fair value being recognized through the consolidated statements of operations until the 2019 Notes were settled. The fair value of the 2019 Notes was determined to be $39.6 million on issuance and $49.4 million as of April 1, 2019, the settlement date. For the year ended December 31, 2019, the Company recognized $9.8 million of expense as changes in fair value and $0.2 million of interest expense.

Revolving Line

On June 23, 2020, the Company and Pacific Western Bank ("Bank") entered into the Third Amendment to Loan and Security Agreement to the revolving line of credit agreement dated as of May 15, 2019 (as amended, the "Pacific Western Loan").

The aggregate availability under the Pacific Western Loan is $30.0 million. The Pacific Western Loan matures on June 23, 2023 as a result of the events discussed in Note 14, Subsequent Events. All outstanding principal amounts are due on the maturity date. The Company must also maintain an aggregate balance of unrestricted cash at Bank (not including amounts in certain specified accounts) equal to or greater than $10.0 million.

The interest rate under the Pacific Western Loan is a variable annual rate equal to the greater of (a) 2.75% above the Prime Rate (as defined in the Pacific Western Loan), or (b) 6.00%. There have been no borrowings under the Pacific Western Loan as of the date of this Annual Report on Form 10-K. The Company was in compliance with its financial covenants under the Pacific Western Loan as of December 31, 2020.

NOTE 10: INCOME TAXES

The Company recorded no federal income tax expense and due to the operating losses incurred for the years ended December 31, 2020 and December 31, 2019. The Company recorded less than $0.1 million and no state income expense for the years ended December 31, 2020 and December 31, 2019, respectively.

Significant components of the Company's deferred tax assets and deferred tax liabilities are as follows (in thousands):

	Years Ended December 31,	
	2020	2019
Noncurrent deferred tax assets:		
Net operating loss carryforwards	$ 39,264	$ 23,358
Contribution carryforwards	39	34
Deferred rent	—	1,099
Lease liability	2,336	—
Deferred revenue	18,684	13,172
Other assets	5,015	2,444
Tax credits	15,959	9,090
Less: valuation allowance	(79,273)	(47,734)
Total deferred tax assets, noncurrent	2,024	1,463
Noncurrent deferred tax liability:		
Property and equipment	601	1,463
Right of use asset	1,423	—
Total deferred tax liabilities, noncurrent	2,024	1,463
Net deferred tax assets	$ —	$ —

As of December 31, 2020 and December 31, 2019, the Company has provided a valuation allowance for the full amount of the net deferred tax assets as the realization of the net deferred tax assets is not determined to be more likely than not. The net increase in the valuation allowance for the year ended December 31, 2020 of $31.5 million is comprised of an increase in the valuation allowance recorded against the deferred tax assets, primarily related to tax credits and net operating loss carryforwards for the year.

The reasons for the difference between actual income tax benefit for the years ended December 31, 2020 and December 31, 2019 and the amount computed by applying the statutory federal income tax rate to losses before income tax benefit are as follows (in thousands):

	Year Ended December 31, 2020		Year Ended December 31, 2019	
	Amount	% of Pre-Tax Earnings	Amount	% of Pre-Tax Earnings
Income tax expense at statutory rate	$ (22,887)	21.0%	$ (19,505)	21.0%
State income taxes, net of federal tax benefit	(1,309)	1.2%	(1,827)	2.0%
Non-deductible expenses	(963)	0.9%	1,784	(1.9%)
R&D and orphan drug credits	(6,869)	6.3%	(4,810)	5.1%
Other	7	0.1%	(639)	0.7%
Change in state tax rate	512	(0.6%)	—	0.0%
Change in valuation allowance	31,532	(28.9%)	24,997	(26.9%)
Income tax (benefit) expense	$ 23	0.0%	$ —	—

As of December 31, 2020, the Company had federal, state, and foreign net operating loss ("NOL") carryforwards of approximately $172.7 million, $116.5 million, and $0.6 million respectively. As of December 31, 2019, the Company had federal, state, and foreign NOL carryforwards of approximately $101.3 million, $101.7 million, and $0.4 million, respectively. Federal NOL carryforwards of $19.7 million begin to expire in 2030 while the remaining federal NOL carryforward of $153.0 million carries forward indefinitely. The state NOL carryforwards begin to expire in 2025. The foreign NOLs carryforward indefinitely. At December 31, 2020, the Company had federal and state research and development ("R&D") tax credits of $9.9 million and an amount less than $0.1 million, which begin to expire in 2027 and 2030, respectively. At December 31, 2019, the Company had federal and state tax R&D credits of $7.2 million and an amount less than $0.1 million which begin to expire in 2027 and 2030, respectively. As of December 31, 2020 and December 31, 2019, the Company had federal Orphan Drug credits of $6.0 million and $1.8 million, respectively, which begin to expire in 2038. At December 31, 2020 and December 31, 2019, the Company had federal contribution carryforwards of $0.2 million and $0.1 million, respectively, which begin to expire in 2021.

The Company incorporated a subsidiary in Australia in 2018. However, the subsidiary has had minimal losses since inception. As such, there are no undistributed earnings as of December 31, 2020 and December 31, 2019.

The Company incorporated a subsidiary in the United Kingdom in 2019. However, the subsidiary has had minimal activity since inception. As such, there are no undistributed earnings as of December 31, 2020 and December 31, 2019.

The Company's ability to utilize its NOL and R&D credit carryforwards may be substantially limited due to ownership changes that may have occurred or that could occur in the future, as required by Section 382 of the Internal Revenue Code of 1986, as amended (the Code), as well as similar state provisions. These ownership changes may limit the amount of NOL and R&D credit carryforwards that can be utilized annually to offset future taxable income and tax, respectively. In general, an "ownership change," as defined by Section 382 of the Code, results from a transaction or series of transactions over a three-year period resulting in an ownership change of more than 50 percent of the outstanding stock of a company by certain stockholders or public groups. The Company has not completed a study to assess whether one or more ownership changes have occurred since the Company became a loss corporation under the definition of Section 382. If the Company has experienced an ownership change, utilization of the NOL or R&D credit carryforwards would be subject to an annual limitation, which is determined by first multiplying the value of the Company's stock at the time of the ownership change by the applicable long-term, tax-exempt rate, and then could be subject to additional adjustments, as required. Any such limitation may result in the expiration of a portion of the NOL or R&D credit carryforwards before utilization. Until a study is completed and any limitation known, no amounts are being considered as an uncertain tax position or disclosed as an unrecognized tax benefit. Any carryforwards that expire prior to utilization as a result of such limitations will be removed from deferred tax assets with a corresponding reduction of the valuation allowance. Due to the existence of the valuation allowance, it is not expected that any possible limitation will have an impact on the results of operations of the Company.

The Company reflects in the accompanying consolidated financial statements the benefit of positions taken in a previously filed tax return or expected to be taken in a future tax return only if it is considered 'more-likely-than-not' that the position taken will be sustained by the appropriate taxing authority. As of December 31, 2020 and December 31, 2019, the Company had no unrecognized income tax benefits. The Company's policy for recording interest and penalties relating to uncertain income tax positions is to record

them as a component of income tax expense in the accompanying consolidated statements of operations. As of December 31, 2020 and December 31, 2019, the Company had no such accruals.

The Tax Cuts and Jobs Act of 2017 subjects a U.S. shareholder to tax on global intangible low-taxed income ("GILTI") earned by certain foreign subsidiaries. The FASB Staff Q&A, Topic 740, No. 5, *Accounting for Global Intangible Low-Taxed Income*, states that an entity can make an accounting policy election to either recognized deferred taxes for temporary basis differences expected to reverse as GILTI in future years or to provide for the tax expense related to GILTI in the year the tax is incurred as a period expense only. The Company has elected to account for GILTI in the year the tax is incurred. The Company does not have a GILTI inclusion in years ends December 31, 2020 or December 31, 2019 and therefore, no GILTI tax has been recorded for the years then ended.

NOTE 11: FAIR VALUE MEASUREMENTS

The carrying amounts of the Company's financial instruments, including accounts receivable, accounts payable, and accrued expenses and other current liabilities, approximate their respective fair values due to their short-term nature. The Company uses a three-tier fair value hierarchy to classify and disclose all assets and liabilities measured at fair value on a recurring basis and to minimize the use of unobservable inputs when determining their fair value. The three tiers are defined as follows:

Level 1—Observable inputs based on unadjusted quoted prices in active markets for identical assets or liabilities

Level 2—Inputs, other than quoted prices in active markets, that are observable either directly or indirectly

Level 3—Unobservable inputs for which there is little or no market date, which require the Company to develop its own assumptions

The Company classifies investments in money market funds within Level 1 as the prices are available from quoted prices in active markets. Investments in repurchase agreements are classified within Level 2 as these instruments are valued using observable market inputs including reported trades, broker/dealer quotes, bids and/or offers.

As of December 31, 2020, the Company held an insignificant amount of cash equivalents. As of December 31, 2019, the Company held cash equivalents which were composed of money market funds and repurchase agreements that were purchased through repurchase intermediary banks and collateralized by deposits in the form of government securities and obligations.

The following represents assets measured at fair value on a recurring basis by the Company (in thousands):

December 31, 2020	Fair Value	Level 1	Level 2	Level 3
Assets:				
Money market funds	$ 10	$ 10	$ —	$ —
Repurchase agreements	—	—	—	—
	$ 10	$ 10	$ —	$ —

December 31, 2019	Fair Value	Level 1	Level 2	Level 3
Assets:				
Money market funds	$ 3,395	$ 3,395	$ —	$ —
Repurchase agreements	173,000	—	173,000	—
	$ 176,395	$ 3,395	$ 173,000	$ —

NOTE 12: COLLABORATION AND LICENSE AGREEMENTS

Development and Commercial License Agreement with Servier

On February 24, 2016, the Company entered into a development and commercial license agreement, as subsequently amended, with predecessor entities to Servier. This agreement establishes a collaboration between the Company and Servier to develop allogeneic chimeric antigen receptor T ("CAR T") cell therapies for up to six unique antigen targets selected by Servier. Servier selected one target at the agreement's inception and, in 2020, selected two additional hematological cancer targets beyond CD19 and two new solid tumor targets. Servier is required to make a milestone payment to the Company upon achievement of an early-stage pre-investigational new drug application ("IND") development milestone event completed for each of the four targets selected after execution of the contract. The Company granted Servier a development license and will perform early-stage R&D on the selected targets and develop the resulting therapeutic product candidates through Phase 1 clinical trials and manufacture clinical trial material

for use in Phase 2 clinical trials. Also, the Company and Servier have formed a joint steering committee ("JSC") to provide high-level oversight and decision making regarding the activities covered under the agreement.

The Company received an upfront payment of $105.0 million under the agreement in 2016. At the Phase 2 readiness stage for any product candidate, Servier may exercise a commercial option, subject to payment of commercial option exercise fees, to proceed with development and commercialization of the product candidate and perform late-stage R&D, including Phase 2 and Phase 3 clinical trials and obtaining regulatory approvals. The Company has the ability to receive total payments, in the aggregate across all five targets selected by Servier, of up to approximately $1.4 billion, including the upfront payment of $105.0 million and up to $1.3 billion in milestone payments, consisting of up to $329.3 million in development milestone payments and up to $925.0 million in commercial milestone payments. The Company is also entitled to receive tiered royalties ranging from the mid-single digit percentages to the sub-teen percentages on worldwide net sales of any products developed, subject to customary potential reductions. The Company also has the right to opt in and participate in the development and commercialization of any products resulting from the collaboration through a 50/50 co-development and co-promotion option in the United States. This will require the Company to pay a co-development and co-promotion option fee on each licensed product for which the Company elects to participate. This option is exercisable at the Phase 2 readiness stage and only after Servier exercises its commercial option.

The Company assessed this arrangement in accordance with ASC 606 and concluded that the promises in the agreement represent transactions with a customer. The Company has determined that the promises associated with the research and development activities for each of the five targets are not distinct because they are all based on the ARCUS proprietary genome editing platform. The Company has concluded that the agreement with Servier contains the following promises: (i) a development license; (ii) performance of early-stage R&D services, (iii) the manufacture of clinical trial material for use in Phase 2 clinical trials, and (iv) JSC participation. The Company determined that the license, manufacture of clinical trial material, and R&D services were not distinct from each other, as the license, pre-clinical and clinical supply, and R&D services are highly interdependent upon one another. Participation on the JSC to oversee the research and development activities are combined into the single performance obligation as these activities are highly interdependent with the other R&D services. As such, the Company determined that these promises should be combined into a single performance obligation.

Under the agreement with Servier, in order to evaluate the appropriate transaction price, the Company determined that the upfront amount of $105.0 million constituted the entire consideration to be included in the transaction price as of the outset of the arrangement. As such, this amount was allocated to the single performance obligation. The commercial option exercise fees that may be received are excluded from the transaction price until each customer option is exercised as it was determined that the options are not material rights. The potential development milestone payments that the Company is eligible to receive prior to the exercise of the options as well as commercial milestones, were excluded from the transaction price at the outset of the arrangement, as all milestone amounts were fully constrained based on the probability of achievement, since the milestones relate to successful achievement of certain developmental goals, which might not be achieved. None of the future royalty payments were included in the transaction price, as the potential payments represent sales-based consideration. The Company will reevaluate the transaction price, including all constrained amounts, at the end of each reporting period and as uncertain events are resolved or other changes in circumstances occur, and, if necessary, adjust its estimate of the transaction price.

The Company recognizes revenue from the upfront payment of $105.0 million and variable consideration related to development milestones achieved on an input method in the form of research effort relative to expected research effort at the completion of the performance obligation, which is based on the actual time of R&D activities performed relative to expected time to be incurred in the future to satisfy the performance obligation. Management evaluates and adjusts the total expected research effort for the performance obligation on a quarterly basis based upon actual research accomplishments and the probability of continuing research efforts in the future. The transfer of control occurs over this time period and, in management's judgment, is the best measure of progress towards satisfying the performance obligation. The remaining performance obligation is expected to be satisfied over approximately a five year period as of December 31, 2020.

During the years ended December 31, 2020 and December 31, 2019, the Company recognized revenue under the agreement with Servier of approximately $18.0 million and $7.3 million, respectively. Deferred revenue related to the agreement with Servier amounted to $82.9 million and $80.9 million as of December 31, 2020 and December 31, 2019, respectively, of which $28.9 million and $15.0 million, respectively, is included in current liabilities.

Collaboration and License Agreement with Gilead

On July 6, 2020 (the "Termination Notice Date"), Gilead Sciences ("Gilead") notified the Company of its termination of the Collaboration and License Agreement between Gilead and the Company, dated September 10, 2018, as subsequently amended by Amendment No. 1 to the Collaboration and License Agreement, dated March 10, 2020 (as amended, the "Gilead Agreement"). Pursuant to the termination notice, the Gilead Agreement terminated on September 4, 2020, upon which the Company regained full

rights and all data it generated for the *in vivo* chronic hepatitis B virus ("HBV") program developed under the Gilead Agreement. The Company is exploring partnership or alternative opportunities to enable the continued development of ARCUS-based HBV therapies, the progression toward the submission of an IND for this product candidate and the reassessment of the timing of such IND submission.

Revenue associated with the combined performance obligation was recognized on a straight-line basis as the R&D services were provided through the Termination Notice Date. During the years ended December 31, 2020 and 2019, the Company recognized revenue under the Gilead Agreement of approximately $3.9 million and $13.3 million, respectively. The Company did not have deferred revenue related to the Gilead Agreement as of December 31, 2020. Deferred revenue was $1.5 million as of December 31, 2019. No development or sales-based milestone payments were received during the twelve months ended December 31, 2020.

NOTE 13: SEGMENT REPORTING

The Company has developed a genome editing platform and performed related research for human therapeutic and agricultural applications. The Company's Chief Operating Decision Maker ("CODM") evaluates the Company's financial performance based on two reportable segments: Therapeutics and Food. The Therapeutics segment is focused on the development of products in the field of immuno-oncology and of novel products outside immuno-oncology to treat human diseases. The Food segment is focused on applying ARCUS to develop food and nutrition products through collaboration agreements with consumer-facing companies. The CODM reviews segment performance and allocates resources based upon segment revenue and segment operating loss of the Therapeutics and Food reportable segments.

Segment operating loss is derived by deducting operational cash expenditures, net, from GAAP revenue. Operational cash expenditures are cash disbursements made that are directly attributable to the reportable segment (including directly attributable research and development and property, equipment, and software expenditures). The Company previously allocated centralized research and development expenditures for early stage research, nuclease development and the purchase of general laboratory supplies to the Therapeutics and Food segments based on headcount and presented such allocated expenditures separately from segment operational cash expenditures. Beginning January 1, 2020, such allocated expenditures are included within segment operational cash expenditures. Prior period information was presented consistent with the current period presentation. In January 2019, the Food segment moved into a new leased facility at Research Triangle Park, North Carolina. The Company determined that the Food segment is no longer deriving benefit from the Company's centralized research and development expenditures for early stage research, nuclease development and the purchase of general laboratory supplies and, as such, all these expenditures are allocated to the Therapeutics segment. Certain reclassifications have been made to the presentation of reportable segments as centralized research and development expenditures are no longer reported separately. The reportable segment operational cash expenditures include cash disbursements for compensation, laboratory supplies, purchases of property, equipment and software and procuring services from CROs, CMOs and research organizations.

Certain cost items are not allocated to the Company's reportable segments. These cost items primarily consist of compensation and general operational expenses associated with the Company's executive, business development, finance, operations, human resources and legal functions. The Company does not allocate non-cash income statement amounts to its reportable segments, such as share based compensation, depreciation and amortization, intangible asset impairment charges, non-cash interest expense and losses on the disposal of assets. When reconciling segment operating loss to consolidated loss from operations, the Company makes an adjustment to convert the cash expenditures to the accrual basis to reflect GAAP.

All segment revenue is earned in the United States and there are no intersegment revenues. Additionally, the Company reports assets on a consolidated basis and does not allocate assets to its reportable segments for purposes of assessing segment performance or allocating resources.

Presented below is the financial information with respect to the Company's reportable segments:

(in thousands)	For the Years Ended December 31, 2020	2019
Revenue:		
Therapeutics	$ 21,863	$ 20,632
Food	2,422	1,606
Total segment revenue	24,285	22,238
Segment operational cash expenditures:		
Therapeutics	$ 71,841	$ 70,059
Food	7,587	6,984
Total segment operational cash expenditures	79,428	77,043
Segment operating loss:		
Therapeutics	$ (49,978)	$ (49,427)
Food	(5,165)	(5,378)
Total segment operating loss	$ (55,143)	$ (54,805)
Adjustments to reconcile segment operating loss to consolidated loss from operations		
Corporate general and administrative cash expenditures	$ (30,090)	$ (32,569)
Interest income received included in segment operating loss	(822)	(4,267)
Depreciation and amortization	(8,777)	(5,317)
Amortization of right-of-use asset	(1,036)	-
Share-based compensation	(13,786)	(8,940)
Loss on disposal of assets	35	(22)
Adjustments to reconcile cash expenditures to GAAP expenses	(209)	18,716
Total consolidated loss from operations	$ (109,828)	$ (87,204)

Note 14: Subsequent Events

Closing of Development and License Agreement and Stock Purchase Agreement with Eli Lilly and Company

On January 6, 2021, the Company and Eli Lilly and Company ("Lilly") closed their previously announced Development and License Agreement ("the Development and License Agreement") following clearance under the Hart-Scott Rodino Antitrust Improvements Act of 1976, as amended (the "HSR Act") and completed the transactions under their previously announced Stock Purchase Agreement (the "Stock Purchase Agreement"). In connection with the closing, the Company received an upfront cash payment of $100.0 million pursuant to the Development and License Agreement and received $35.0 million from Lilly's purchase of 3,762,190 newly issued shares of the Company's common stock pursuant to the Stock Purchase Agreement.

Under the Development and License Agreement, the Company will collaborate with Lilly to discover and develop *in vivo* gene editing products incorporating the Company's ARCUS nucleases. Lilly has initially nominated Duchenne muscular dystrophy and two gene targets for other genetic disorders, and has the right to nominate up to three additional gene targets for genetic disorders over the first four years of the Development and License Agreement (the "Nomination Period"). Lilly may extend the Nomination Period for an additional two years from the date on which such initial Nomination Period ends, upon Lilly's election and payment of an extension fee. Under the terms of the Development and License Agreement, Lilly will receive an exclusive license to research, develop, manufacture and commercialize the resulting licensed products to diagnose, prevent and treat any and all diseases by in vivo gene editing directed against the applicable gene target. The Development and License Agreement provides that the Company will be responsible for conducting certain pre-clinical research and IND-enabling activities with respect to the gene targets nominated by Lilly to be subject to the collaboration, including manufacture of initial clinical trial material for the first licensed product. Lilly will be responsible for, and must use commercially reasonable efforts with respect to, conducting clinical development and commercialization activities for licensed products resulting from the collaboration, and may engage the Company for additional clinical and/or initial commercial manufacture of licensed products.

Pursuant to the Development and License Agreement, the Company will also be eligible to receive milestone payments of up to an aggregate of $420.0 million per licensed product as well as nomination fees for additional targets and certain research funding. If licensed products resulting from the collaboration are approved and sold, the Company will also be entitled to receive tiered royalties ranging from the mid-single digit percentages to the low-teens percentages on world-wide net sales of the licensed products, subject to customary potential reductions. Lilly's obligation to pay royalties to the Company expires on a country-by-country and licensed

product-by-licensed product basis, upon the latest to occur of certain events related to expiration of patents, regulatory exclusivity or a period of ten years following first commercial sale of the licensed product. No revenue was recognized under the Development and License agreement in the twelve months ended December 31, 2020.

Duke License

As a result of the closing of the Development and License Agreement in January 2021, we will be required to make payments under the Duke License of $3.0 million in 2021, net of any outstanding credits.

Extension of Maturity date of Revolving Line with Pacific Western bank

Pursuant to the terms of the Pacific Western Loan regarding the Company receiving cash from the issuance of the Company's equity securities and/or from strategic partnerships, the maturity date of the Revolving Line was extended from June 23, 2022 to June 23, 2023 as a result of the proceeds received from Lilly in connection with the closing of the Development and License Agreement and Stock Purchase Agreement in January 2021.

[THIS PAGE INTENTIONALLY LEFT BLANK]

Executive Officers

Matthew Kane
President, Chief Executive Officer and Director

Derek Jantz, Ph.D.
Chief Scientific Officer and Director

Alex Kelly
Interim Chief Financial Officer

Christopher Heery, M.D.
Chief Medical Officer

Dario Scimeca
General Counsel and Secretary

Fayaz Khazi, Ph.D.
Chief Executive Officer, Elo Life Systems

David Thomson, Ph.D.
Chief Operating Officer

Board of Directors

Kevin J. Buehler
Chairman of the Board of Directors, Former Division Head, Alcon Laboratories Inc.

Geno Germano
President and Chief Executive Officer, Elucida Oncology, Inc.

Derek Jantz, Ph.D.
Chief Scientific Officer, Precision BioSciences, Inc.

Matthew Kane
President and Chief Executive Officer, Precision BioSciences, Inc.

Raymond Schinazi, Ph.D., D.Sc
Frances Winship Walters Professor of Pediatrics and Director of Laboratory of Biochemical Pharmacology, Emory University

Shalini Sharp
Former Executive Vice President and Chief Financial Officer, Ultragenyx Pharmaceutical Inc.

Tony Yao, M.D., Ph.D.
Portfolio Manager, ArrowMark Partners

Corporate and Stockholder Information

Corporate Headquarters
Precision BioSciences, Inc.
302 East Pettigrew Street, Suite A-100
Durham, North Carolina 27701
www.precisionbiosciences.com

Transfer Agent
American Stock Transfer & Trust Company
6201 15th Avenue
Brooklyn, NY 11219
Phone: 800.937.5449
www.amstock.com

Investor Relations
Alex Kelly
Interim Chief Financial Officer
Maurissa Messier
Senior Director, Corporate Communications
IR@precisionbiosciences.com

Annual Meeting of Stockholders
Monday, May 10, 2021
11:00 a.m., Eastern Time
Via live webcast

Common Stock Listing
Nasdaq: DTIL

Corporate Counsel
Latham & Watkins LLP
885 Third Avenue
New York, NY 10022-4834
Phone: 212.906.1200
www.lw.com

Independent Registered Public Accounting Firm
Deloitte & Touche LLP

PRECISION
BIOSCIENCES

302 East Pettigrew St.
Suite A-100
Durham, NC 27701

www.precisionbiosciences.com