Fiscal Year

2022 ANNUAL REPORT

PRECISION BIOSCIENCES

Statements in this letter regarding the Company's planned strategy, business focus and intended product development, are forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. These forward-looking statements speak only as of the date such statements are made and are subject to risks and uncertainties that could cause the Company's results to differ materially from these statements. These risks and uncertainties are described in the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2022 under the caption “Risk Factors,” as such factors may be updated from time to time in the Company's other filings with the SEC. All forward-looking statements speak only as of the date of this letter and, except as required by applicable law, the Company does plan to publicly update or revise any such forward-looking statements, whether as a result of any new information, future events, changed circumstances or otherwise.

Dear Fellow Stockholders:

Since our founding, we have maintained steadfast dedication to improving life for patients in need, by translating the immense potential of genome editing into curative therapeutic solutions. Underlying this mission is the belief that core features of ARCUS differentiate our wholly owned platform in safety, specificity, versatility and delivery of genomic edits, with the potential for an extensive reach across underserved markets in oncology and blood disorders, severe genetic disease and even infectious disease, like chronic hepatitis B virus. Reflecting on our recent progress and looking ahead for Precision BioSciences, our platform and mission serve as guideposts as we set and execute a strategy that positions our company for the long term.

2022 was a significant year for Precision. We made meaningful strides with our diversified pipeline through the following:

- Generated new preclinical data that have been instrumental in refining our *in vivo* gene editing portfolio strategy.
- Established a new, premium *in vivo* gene editing collaboration with Novartis, focused on gene insertion for sickle cell disease and beta thalassemia.
- Reported encouraging response rates in the azercabtagene zapreleucel (azer-cel) Phase 1b clinical study, in patients that have failed treatment with autologous CAR T therapies.
- Progressed the Phase 1 study of our stealth cell candidate, PBCAR19B.
- Invested in platform-wide optimizations to manufacturing of our *ex vivo* allogeneic CAR T product candidates, and engaged with regulators in support of our next steps towards patients.

In addition, we have made considerable operational progress that we believe has strengthened our corporate position. We extended our anticipated cash runway through the first quarter of 2025, in part through pairing proceeds from our June financing with collaboration revenue and fiscal discipline to withstand the challenging conditions of today's market. We have also continued to fortify our management and Board with new perspectives and diverse experience across functions critical to support Precision's growth. We hired Juli Blanche, a seasoned human resource executive, as Chief People Officer; promoted our in-house Chemistry, Manufacturing and Controls (CMC) expert Neil Leatherbury to Senior Vice President, Head of CMC, and Jeff Smith, Ph.D., one of the true pioneers in genome editing as an ARCUS inventor and Precision co-founder, to Chief Research Officer; and added proven financial expert Melinda Brown as our sixth independent director to the Board of Directors. With her appointment as Audit Committee Chair along with the appointment of Shari Piré as the

Nominating and Governance Chair, half of the Board committees are now chaired by women. Altogether, this reflects our conviction that investing in strong leadership and good governance spanning key capabilities end to end, from research to commercialization, will position Precision for its future as a leading gene editing company.

To that end, we expect that 2023 will be transformative for Precision. Across our portfolio, we will continue to sharpen focus on disease areas where we believe ARCUS, more than any other technology, can have the greatest and most profound impact. For our *in vivo* pipeline, we have long believed this differentiation lies in high-efficiency gene insertion and complex edits, aimed at restoring genomic function and treating the underlying root cause of specific genetic diseases. We expect emerging preclinical data and market analysis to inform continued prioritization of our internal efforts alongside progression of our partnered programs, including the first ARCUS nuclease for *in vivo* gene insertion planned to move towards regulatory submission. Further, we expect that clinical results will guide next steps for azer-cel and PBCAR19B, respectively, as potential first-in-class and best-in-class CD19-targeted allogeneic CAR T solutions, if approved. We look forward to sharing these and many more developments that we believe will advance our vision and shape the next phase of our company's growth.

Lastly, I want to extend my gratitude – to our remarkable team of Precisioneers, for their consistent and unwavering dedication to our mission; to our research partners and clinical collaborators, and especially patients and their families, for their belief in ARCUS and trust in Precision; and to our loyal stockholders, whose support has been instrumental in our progress to date and enables us to build Precision for tomorrow.

Warm Regards,

Michael Amoroso

Chief Executive Officer

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

FORM 10-K

(Mark One)

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the fiscal year ended December 31, 2022
OR

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the transition period from to
Commission File 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, a 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 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, 2022, was $170.3 million.

The number of shares of Registrant's common stock outstanding as of March 1, 2023 was 111,295,723.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive proxy statement for its 2023 annual stockholders' meeting, which is to be filed within 120 days of the registrant's fiscal year ended December 31, 2022, are incorporated by reference into Part III of this Annual Report on Form 10-K.

Auditor Firm Id: 34 Auditor Name: Deloitte & Touche LLP Auditor Location: Raleigh, North Carolina

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, use and development of Licensed Products (as defined herein), planned preclinical studies and clinical trials, or discontinuance thereof, the status and results of our preclinical and clinical studies, including, the potential of our product candidates, if approved, to become best-in-class or first-in-class, 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, collaborations and potential new partnerships or alternative opportunities for our product candidates, capabilities of our manufacturing facility, potential new application filings and 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 and variants thereof 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 limited ability or inability to assess the safety and efficacy of our product candidates;
- the risk that other genome-editing technologies may provide significant advantages over our ARCUS technology;
- our dependence on our ARCUS technology;
- the initiation, cost, timing, progress, achievement of milestones and results of research and development activities and preclinical and clinical studies;
- public perception about genome editing technology and its applications;
- competition in the genome editing, biopharmaceutical, and biotechnology fields;
- our or our collaborators' ability to identify, develop and commercialize product candidates;
- pending and potential product 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 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" and initial 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 protection, privacy and security regulations and our compliance therewith;
- our ability to obtain orphan drug designation or fast track designation for our product candidates or to realize the expected benefits of these designations;
- 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;
- the rate and degree of market acceptance of any of our product candidates;
- our ability to effectively manage the growth of our operations;
- our ability to attract, retain, and motivate executives and personnel;
- effects of system failures and security breaches;
- insurance expenses and exposure to uninsured liabilities;
- effects of tax rules;
- effects of the COVID-19 pandemic and variants thereof, or any pandemic, epidemic, or outbreak of an infectious disease;
- the success of our existing collaboration agreements and our ability to enter into new collaboration arrangements;
- our current and future relationships with and reliance on 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;
- effects of natural and manmade disasters, public health emergencies and other natural catastrophic events;
- effects of sustained inflation, supply chain disruptions and major central bank policy actions;
- market and economic conditions; 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 former 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 not been profitable and may not 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 three 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, 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.*
- *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.*
- *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.*
- *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.*
- *Our future success depends on our key executives, as well as attracting, retaining and motivating qualified personnel.*
- *COVID-19 has impacted, and may continue to impact, 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

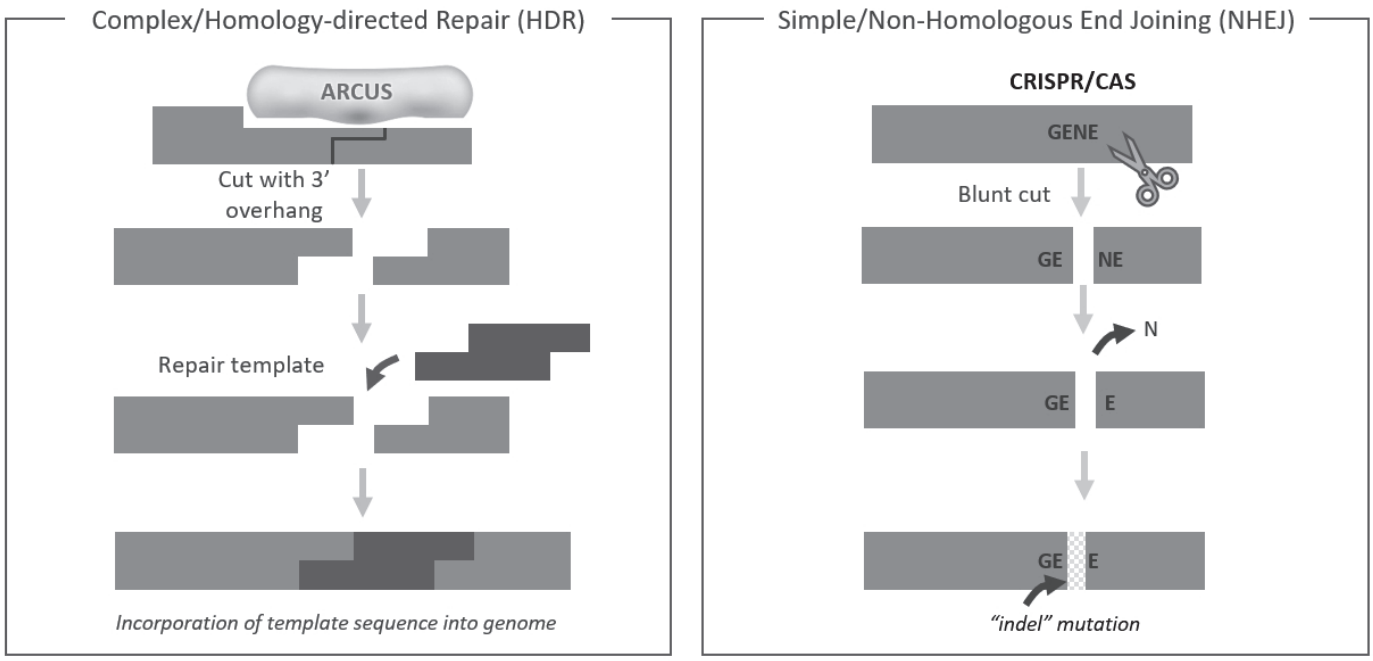
Item 1. Business.

We are a clinical stage gene editing company dedicated to improving life by developing *ex vivo* allogeneic chimeric antigen receptor ("CAR") T immunotherapies and *in vivo* therapies for genetic and infectious diseases with the application of our wholly owned proprietary ARCUS genome editing platform. The foundation of ARCUS is a natural homing endonuclease which allows us to replicate precise gene editing as it evolved in nature. ARCUS is designed to be precise in its specificity and versatile in its design for gene knock out as well as complex edits with gene insertion and gene repair. ARCUS is also unique in its relatively small size which potentially allows delivery to a wider range of cells and tissues using viral and non-viral gene delivery methods.

Overview of Genome Editing

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 aberrations 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 ("NHEJ"), and homology directed repair ("HDR"). As shown in the figure 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, "knock out", or alter 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 the figure 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 inserted 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. ARCUS cuts with a three prime, or 3', overhang which are unique and designed to enable gene insertion and complex edits, and provide an identifiable signature for on-target editing.

There are several genome editing technologies, including ARCUS, zinc-finger nucleases ("ZFNs"), TAL-effector nucleases ("TALENs"), CRISPR/Cas9, and base editors. 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 ARCUS Genome Editing Platform

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:

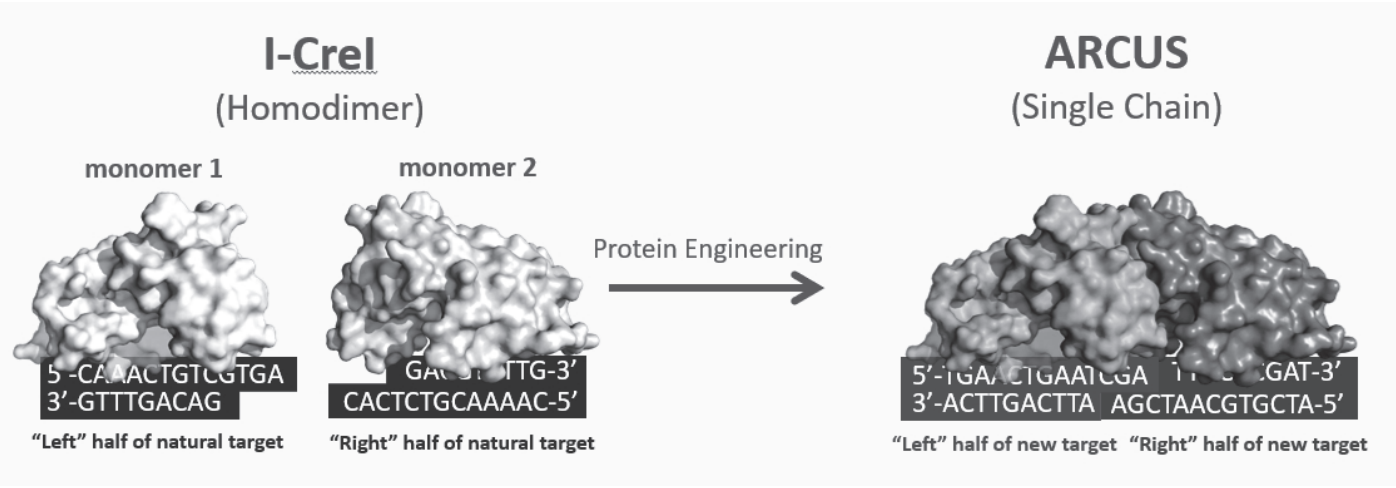
- **Specificity and efficiency.** Complex genome editing applications, especially those involving the human body, require a high level of endonuclease specificity and precision to limit the likelihood that the endonuclease will recognize and edit any genetic sequence other than its intended target. Most 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 precise on-target editing while rarely cutting off-target, as supported by scientific literature.
- **Delivery.** Size and structural simplicity affect the ease and versatility 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 3' overhangs created when I-CreI cuts DNA have been shown to promote DNA repair through 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 versatile 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.
- **Intellectual Property.** 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 make 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 17 years of research effort to develop ARCUS, 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.

ARCUS is a collection of protein engineering methods that we developed specifically to re-program the DNA recognition properties of I-CreI, a homing endonuclease from *Chlamydomonas reinhardtii* algae evolved for precision genome editing in nature. 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, 2022, we have obtained U.S. patents with claims directed to eight ARCUS nucleases as compositions of matter, and currently claim over 350 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 an 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.



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 several 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 to one year and results in development of our clinical candidate nuclease.

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.

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 medical needs by leveraging the ARCUS gene editing platform in oncology and genetic diseases. 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.
- **Advance a potential first-in-class and a best-in-class, if approved, allogeneic CAR T treatment for hematologic cancer.** Currently, there are no therapeutics approved by the U.S. Food and Drug Administration ("FDA") for lymphoma patients who have relapsed following autologous CAR T therapy. We believe our lead anti-CD19 allogeneic candidate, azercabtagene zapreleucel ("azer-cel"), has the potential to be a first-in-class treatment for relapsed or refractory ("R/R") non-Hodgkin lymphoma ("NHL") patients who have relapsed post autologous CAR T therapy and are actively enrolling additional NHL patients in this relapsed setting for further evaluation. We expect the CAR T relapsed market for diffuse large B-cell lymphoma ("DLBCL") to grow considerably by 2025, driven by autologous CAR T therapy becoming the second line standard-of-care. In the auto CAR T relapsed patient population, azer-cel has shown high response rates in our mid-2022 clinical results, with evidence of durability extending greater than 18 months and high levels of peak CAR T levels. Manufacturing optimization resulted in improved product attributes supporting the opportunity to reduce lymphodepletion dose in combination with azer-cel, and we received Type C feedback from the FDA on our chemistry, manufacturing and controls ("CMC") strategies supporting ongoing late-stage development for azer-cel. In addition, we are continuing to recruit additional patients for PBCAR19B, our CD19-targeting CAR T cell therapy, in the earlier line R/R DLBCL patients to complete Phase 1.
- **Unlock the full potential of ARCUS *in vivo* gene editing platform.** We aim to differentiate ARCUS on safety, gene insertion, and complex edits and are working toward advancing the first ARCUS-based *in vivo* gene editing programs to the clinic to address serious genetic diseases and chronic hepatitis B. In our preclinical studies, we observed the high-efficiency and tolerability of *in vivo* genome editing using ARCUS in a non-human primate ("NHP") model, as published in *Nature Biotechnology* in July 2018 and *Molecular Therapy* in June 2021 by Wang et al. Over five years later, NHPs in this 2017 study continue to be monitored for ongoing, sustained reduction in LDL cholesterol levels while maintaining stable gene editing and data from these trials has not shown any obvious adverse effects to date. To our knowledge, we were the first company to complete this milestone, which we believe to be critical to successful *in vivo* genome editing therapeutic development.
- **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 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 selective premium *in vivo* gene editing collaborations.** We believe that the ARCUS genome editing platform has broad utility beyond our current areas of focus. We intend unlock additional development opportunities with companies with additive expertise in areas within and outside of our current target markets to reach more patients and provide capital for advancing our wholly owned programs.

In December 2021, we announced our entry into an agreement with a syndicate of investors led by ACCELR8 to separate our then wholly owned subsidiary, Elo Life Systems, Inc. ("Elo"), to create an independent food and agriculture business ("New Elo").

***Ex vivo* Allogeneic CAR T Immunotherapy Platform**

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. 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 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.

The only commercial form of CAR T cell therapy 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. The therapy is highly personalized, difficult to scale, has an associated high rate of relapse and is expensive. Because of the patient's illness, their cells may also not be suitable starting material for manufacturing. Our allogeneic approach uses donor-derived T cells with a single gene edit using ARCUS that are designed for safe delivery to patients with certain cancers. 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 larger 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. We believe our CAR T cells are the only allogeneic CAR T cells in human clinical trials made with a single gene editing step to specifically avoid the potentially deleterious effects of making multiple edits to T cells. We are simultaneously conducting a Phase 1b/2a clinical trial evaluating azer-cel, as a potential first-in-class, if approved, and a Phase 1 clinical trial evaluating PBCAR19B as a potential best-in-class, if approved, CD19-targeting CAR T cell therapy in adult patients with R/R B-cell malignancies.

In parallel to our development of azer-cel, we are also working towards developing a candidate with an allogeneic CAR T profile that has the potential to displace CD19 directed autologous CAR T for earlier line NHL patients with unique attributes of ARCUS, which is designed to make complex gene edits in a single step with a single dose, potentially reducing translocation safety concerns. We have developed a second-generation "stealth cell" CAR T construct, which we believe has the potential to overcome certain limitations of rejection of allogeneic CAR T cells by the patient's immune system. Rejection of allogeneic CAR T cells could limit the efficacy of a CAR T therapy if the cells do not persist long enough in the patient to eradicate the tumor. PBCAR19B is an anti-CD19 CAR T candidate built on the stealth cell platform utilizing a single-step gene edit in an effort to minimize the risk of chromosome abnormalities. The stealth cell differs from azer-cel in that it has two additional modifications aimed at avoiding rejection. The stealth cell technology is a modified CAR T vector that is designed to suppress expression of a gene called β2m, in CAR T cells using a short-hairpin RNA, or shRNA, and enable expression of a transgenic HLA-E molecule on the cell surface. β2m 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 β2m 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 β2m 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 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.

With our decision early in the development of our *ex vivo* platform to invest in process development, we continue to scale and improve our manufacturing process and are currently producing allogeneic CAR T cells at scale for clinical trials in accordance with current good manufacturing practice ("cGMP").

***Ex vivo* Allogeneic CAR T Immunotherapy Pipeline**

Azer-cel. We are conducting our Phase 1b/2a clinical trial of azer-cel in adult patients with R/R NHL. Made from donor-derived T cells modified using our ARCUS genome editing technology, azer-cel recognizes the well characterized tumor cell surface protein

CD19, an important and validated target in several B-cell cancers. Azer-cel is designed to avoid graft-versus-host disease, a significant complication associated with donor-derived, cell-based therapies. In June 2022, we provided an interim clinical update and outlined the opportunity for azer-cel for the growing CAR T relapsed patient population with aggressive lymphomas. As of the May 31, 2022 data cutoff, positive efficacy results, including high overall response rate ("ORR") and complete response ("CR") rates and duration of response, and an improved adverse event profile have been observed among evaluable CAR T relapsed subjects. This included six subjects who received azer-cel Dose Level ("DL") 3 of 3×10^6 cells/kg with enhanced lymphodepletion of fludarabine 30 mg/m^2/day × 4 days + cyclophosphamide 1000 mg/m^2/day × 3 days (the "ASH Cohort") and six subjects who received azer-cel DL4b, a flat dose of 500×10^6 cells, with reduced dose lymphodepletion of fludarabine 30 mg/m^2/day × 4 days + cyclophosphamide 750 mg/m^2/day × 3 days since January 2022 (the "New Cohort"). Among 11 subjects evaluable for response, the program update reported efficacy results across both the ASH Cohort and New Cohort, including a 100% (11/11) ORR and 73% (8/11) CR rate. Six subjects were in ongoing response (up to 18+ months). In the ASH Cohort, 50% (3/6) of evaluable subjects had a response duration greater than six months. Among subjects treated with DL4b and reduced intensity lymphodepletion in the New Cohort, a 100% CR rate was achieved among evaluable subjects (5/5). One subject was non-evaluable at the Day 28 assessment due to death from suspected fludarabine-associated neurotoxicity on Day 23. The subject had complete resolution of disease according to a CT scan on Day 21.

No Grade 3 or greater cytokine release syndrome was observed in either dosing cohort. One Grade 3 immune effector cell-associated neurotoxicity syndrome was recorded in each cohort that rapidly resolved to Grade 1 within 24 to 48 hours. Two Grade 5 events associated with late occurring encephalopathy suspected to be related to fludarabine-associated neurotoxicity occurred in the New Cohort. There was no evidence of graft versus host disease in either cohort. Grade 3 or greater infections occurred less frequently in the New Cohort with one out of six (17%) subjects compared to four out of six (67%) subjects in the ASH Cohort.

A poster presented at the 64th ASH Annual Meeting in December 2022 evaluated the relationship between healthy cell dose and functional attributes of azer-cel to the efficacy and safety of the product in patients with R/R B-cell lymphoma. This poster showed that post-thaw product composition and healthy CAR T cell dose were predictive for response to treatment with azer-cel. Based on these findings, we have applied manufacturing optimizations across all allogeneic CAR T platforms with the goal of improving those product attributes and characteristics that were shown to be able to drive predictability, reliability, and performance.

In January 2023, we announced we received FDA feedback that we believe signaled alignment with our proposed CMC plan for azer-cel. In 2023, we intend to progress azer-cel to a decision point for a Phase 2 trial in NHL subjects who have relapsed following autologous CAR T treatment by completing the Phase 1b cohort to identify a dosing schedule for further study and we plan to seek feedback from the FDA on the azer-cel clinical program once more data become available.

The FDA has granted azer-cel orphan drug designation for the treatment of acute lymphoblastic leukemia ("ALL") and Fast Track Designation for treatment of B-cell precursor acute lymphoblastic leukemia ("B-ALL").

PBCAR19B. As of the June 2022 program update, a flat dose of 270 million cells (DL1) following standard lymphodepletion of fludarabine 30 mg/m^2/day × 3 days + cyclophosphamide 500 mg/m^2/day × 3 days has been administered to three subjects with R/R diffuse large B-cell lymphoma. We are continuing to recruit patients in the PBCAR19B clinical program at DL2 (flat dose of 540 million cells) with the intent to complete the Phase 1 dose escalation in the earlier line NHL setting in 2023.

We plan to provide a CAR T program update once investigators complete enrollment of the current azer-cel cohort of six CAR T relapsed subjects with sufficient follow-up to support a meeting with the FDA to discuss clinical plans. Subjects are being treated with optimized azer-cel product at the planned final dose level (500 million CAR T cells following a lymphodepletion regimen consisting of 3 days of fludarabine and cyclophosphamide). Based on current enrollment, the update is expected to occur in the April/May 2023 time frame, once appropriate follow-up from the current cohort is available. We plan to provide additional long term follow up from the azer-cel cohorts presented at ASH 2021 and ASCO 2022, as well as data from subjects in the current cohort. The CAR T update is also expected to include interim efficacy and safety data from the PBCAR19B Phase 1 trial at Dose Level 2 (540 million CAR T cells following 3 days of fludarabine and cyclophosphamide) with an expectation of durability data to follow this year.

PBCAR269A. PBCAR269A is an investigational allogeneic CAR T cell candidate targeting B-cell maturation antigen ("BCMA") for R/R multiple myeloma in combination with nirogacestat, a gamma secretase inhibitor ("GSI") developed by SpringWorks Therapeutics, Inc. The combination therapy and increased dose of PBCAR269A resulted in improved cell expansion, which correlated with increased clinical activity when compared to dose-matched PBCAR269A monotherapy treatment. However, in light of the competitive landscape of BCMA targeted therapies in multiple myeloma, we have made the strategic decision not to continue the PBCAR269A clinical program. All subjects enrolled in the study and evaluated for treatment with PBCAR269A and nirogacestat had acceptable tolerability results.

***In vivo* Gene Editing Platform**

Our goal with our *in vivo* gene editing programs is to cure genetic diseases by correcting the DNA errors responsible for causing them. 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.

In vivo gene editing is complex and involves the delivery of ARCUS nucleases directly into a patient's cells to treat disease at the level of the underlying DNA. We expect the development of *in vivo* therapies for genetic and infectious diseases to be a significant focus of our operations long-term. We believe these applications are particularly well suited to ARCUS because they require extremely low levels of off-target editing and efficient delivery.

Our ARCUS platform is designed to enable safe, specific and efficient gene editing. Since ARCUS can be delivered via adeno-associated virus ("AAV") or lipid nanoparticle ("LNP"), it has potential utility in treating diseases in the liver as well as many genetic diseases that affect tissues beyond the liver. We believe these unique attributes of ARCUS support its potential differentiation for *in vivo* use and its potential to treat a broader range of genetic diseases than other editing technologies.

We have advanced a deep portfolio of diverse programs toward preclinical efficacy and toxicity studies. We have generated a significant large animal dataset and have observed high-efficiency *in vivo* genome editing in 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. We, along with partners, continue to validate unique features of the ARCUS platform with regards to safety, on-target editing, gene insertion, complex gene edits, and compatibility with viral and non-viral delivery.

The strategic prioritization exercise for our *in vivo* research pipeline, announced in November 2022, is ongoing to assess diseases with highest unmet need in an increasingly dynamic regulatory and competitive gene editing landscape. We are making trade-offs and further honing our focus on disease areas where we believe ARCUS, more than any other technology, can have the greatest and most profound impact. The proof-of-concept preclinical data continues to highlight the unique features of the ARCUS platform supporting prioritization of programs involving complex edits and gene insertion (adding a functional copy of a gene) as exemplified by our partnered neonatal onset ornithine transcarbamylase ("OTC") deficiency program. While we remain committed to patients with cardiovascular diseases, we have made the decision to cease pursuit of PBGENE-PCSK9 for familial hypercholesterolemia ("FH") with iECURE as our partner. PBGENE-PCSK9 for FH remains a wholly-owned program, and we are monitoring the regulatory landscape as we consider FH as well as several potential cardiovascular disease indications in our pipeline prioritization exercise.

***In vivo* Gene Editing Pipeline**

PBGENE-HBV. Our wholly-owned gene editing program for chronic hepatitis B virus ("HBV") applies ARCUS to knock out persistent covalently closed circular DNA ("cccDNA") and potentially reduce viral persistence. In October 2022, we reported preclinical data during an oral presentation at the European Society of Gene & Cell Therapy 29th Congress. This data showed that ARCUS efficiently targeted and degraded HBV cccDNA in HBV-infected primary human hepatocytes and reduced expression of HBV S-antigen ("HBsAg") by as much as 95%. Similar levels of HBsAg reduction were observed in a newly developed mouse model of HBV infection following administration of ARCUS mRNA using LNP delivery. We plan to present additional data at a scientific conference in 2023 and expect to submit a Clinical Trial Application ("CTA") or Investigational New Drug ("IND") application in 2024 for our HBV program.

PBGENE-HbE. In June 2022, we announced we entered into an exclusive in vivo gene editing research and development collaboration and license agreement (the "Novartis Agreement") with Novartis Pharma AG ("Novartis"). In connection with this partnership we are developing a custom ARCUS nuclease that will be designed to insert, *in vivo*, a therapeutic transgene at a "safe harbor" location in the genome as a potential one-time transformative treatment option for diseases including certain hemoglobinopathies such as sickle cell disease and beta thalassemia. ARCUS will be used to add an antisickling gene to hematopoietic stem cells ("HSCs"). We believe permanent integration of an antisickling gene into a "safe harbor" locus in HSCs could prevent the sickle cell phenotype in mature erythrocytes. Under the terms of the Novartis Agreement, we will develop an ARCUS nuclease and conduct *in vitro* characterization, with Novartis then assuming responsibility for all subsequent research, development, manufacturing and commercialization activities.

PBGENE-DMD, PBGENE-LL2 and PBGENE-LL3. We continue our *in vivo* gene editing collaboration with Eli Lilly and Company ("Lilly") in applying ARCUS nucleases to three initial targets, including Duchenne muscular dystrophy ("DMD") in muscle, a liver directed target and a central nervous system directed target. ARCUS genome editing has previously been shown to increase expression of a shortened version of dystrophin in cultured myoblasts from a DMD patient. The approach uses two ARCUS nucleases delivered by a single AAV to simultaneously cut and delete a large segment of the dystrophin gene that encodes exons 45 through 55 of dystrophin – a region of the gene that accounts for more than 50% of DMD-causing mutations.

iECURE-OTC. In partnership with iECURE, Inc. ("iECURE"), an ARCUS-mediated gene insertion approach is being pursued as a potential treatment for OTC deficiency by delivery of dual AAV-based vectors carrying an ARCUS nuclease vector (GTP-506A) and therapeutic donor vector (GTP-506D) via a PCSK9 "safe harbor" site. In October 2022, preclinical data were presented by researchers from the University of Pennsylvania's Gene Therapy Program in collaboration with iECURE at the International Conference on Ureagenesis Defects and Allied Conditions 2022 highlighting an ARCUS-based gene insertion approach for the treatment of OTC deficiency. NHP data demonstrated stable insertion of the therapeutic gene one year post-dosing in newborn and infant NHPs. In the follow up data, 12-month biopsies continued to demonstrate construct stability, with transduction efficiency up to 28.2% as measured by in-situ hybridization. These data further demonstrate the preclinical feasibility of using an ARCUS-mediated gene insertion approach. A CTA and/or IND filing for neonatal onset OTC deficiency is planned for submission in the second half of 2023.

iECURE-OTHER. iECURE uses our PCSK9-directed ARCUS nuclease to develop gene-insertion therapies for other pre-specified rare genetic diseases, including Phenylketonuria and Citrullinemia Type 1.

PBGENE-PH1. Work on the PBGENE-PH1 program progressed as planned in 2022. We have clinical candidates ready to proceed to the next stage of IND enabling studies. Based on our new prioritized focus as well as the evolving treatment paradigm for PH1, we have made the choice to look for a partner in the kidney disease arena for further development of PBGENE-PH1 and will no longer develop the program on our own.

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 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.

We currently contract with third parties for the manufacturing and testing of materials used in the production of our product candidates. To date, our third-party manufacturers have met our manufacturing requirements. Supply chain constraints affecting the industry have also impacted MCAT. Lead times for certain single-use components have been extended but have not materially constrained our ability to produce clinical trial materials to date. In addition to existing supply agreements for our most critical reagents and supplies, we believe that there are alternate sources of supply that can satisfy our requirements and dual sourcing strategies are being employed in select instances to mitigate risk. However, continued global impacts from the COVID-19 pandemic, and other global macroeconomic conditions such as the current inflationary environment, have led to longer timelines and greater costs.

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 single step approach not only minimizes translocation safety concerns, but also 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 editing 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 Team

We believe that our team, whom we call Precisioneers, has among the strongest scientific experience and capabilities of all genome editing companies. Our senior leaders bring extensive experience leading organizations focused on cell and gene therapies with a particular focus on oncology drugs, including CAR T cell therapies for hematologic malignancies, with several who have been working with genome editing technology for approximately 20 years.

We have recruited our team of Precisioneers to include individuals with extensive industry experience and expertise in the discovery, development and manufacture of cell and gene therapies. As of December 31, 2022, our team of Precisioneers included 40 full-time employees with Ph.D. or M.D. degrees.

License and Collaboration Agreements

Novartis Pharma AG

On June 14, 2022, we entered into the Novartis Agreement, which became effective on June 15, 2022 (the "Novartis Effective Date"), to collaborate to discover and develop *in vivo* gene editing products incorporating our custom ARCUS nucleases for the purpose of seeking to research and develop potential treatments for certain diseases (as defined in the Novartis Agreement, the "Licensed Products"). Any initial Licensed Products will be developed for the potential treatment of certain hemoglobinopathies, including sickle cell disease and beta thalassemia.

Pursuant to the terms of the Novartis Agreement, we will develop an ARCUS nuclease and conduct *in vitro* characterization for the Licensed Products, with Novartis then assuming responsibility for all subsequent development, manufacturing and commercialization activities. Novartis will receive an exclusive license for, and be required to use commercially reasonable efforts to conduct all subsequent research, development, manufacture and commercialization activities with respect to the Licensed Products. We will initially develop a single, custom ARCUS nuclease for a defined "safe harbor" target site for insertion of specified therapeutic payloads in the patient's genome (the "Initial Nuclease") for Novartis to further develop as a potential *in vivo* treatment option for certain hemoglobinopathies, including sickle cell disease and beta thalassemia. Pursuant to the terms of the Novartis Agreement, Novartis may elect, subject to payment of a fee to us, to replace Licensed Products based on the Initial Nuclease with Licensed Products based on a second custom ARCUS nuclease we design for gene editing of a specified human gene target associated with hemoglobinopathies (the "Replacement Nuclease"). Additionally, Novartis has the option, upon payment of a fee to us for each exercise of the option, to include Licensed Products utilizing the Initial Nuclease for insertion of up to three additional specified therapeutic payloads at the "safe harbor" target site, each intended to treat a particular genetic disease. The exercise period for such option ends on the earlier of (a) the fourth anniversary of the Novartis Effective Date and (b) the replacement of the Initial Nuclease with the Replacement Nuclease as described above.

In July 2022, we received a $50.0 million upfront cash payment under the Novartis Agreement. Additionally, on the Novartis Effective Date, Novartis made an equity investment in our common stock pursuant to a stock purchase agreement (the "Novartis Stock Purchase Agreement") pursuant to which, on the Novartis Effective Date, we issued and sold to Novartis 12,407,440 shares of our common stock (the "Novartis Shares") in a private placement transaction for an aggregate purchase price of $25.0 million, or approximately $2.01 per share. The price per share of our common stock under the Novartis Stock Purchase Agreement represented a 20% premium over the volume-weighted-average-price of our common stock over the 10 trading days preceding the execution date of the Novartis Stock Purchase Agreement.

We will also be eligible to receive milestone payments of up to an aggregate of approximately $1.4 billion as well as 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 to low-double digit percentages on net sales of Licensed Products, subject to customary potential reductions.

Eli Lilly and Company

In January 2021, we closed a development and license agreement, subsequently amended by the First Amendment to the Development and License Agreement dated August 9, 2021 (as amended, the "Lilly Agreement") with Lilly to utilize ARCUS for the research and development of potential *in vivo* therapies for genetic disorders. Lilly has initially nominated DMD, a liver-directed target and a central nervous system directed target, and has the right to nominate up to three additional gene targets for genetic disorders over the initial nomination period of four years (the "Nomination Period"). Lilly may extend the Nomination Period for an additional two years from the date on which the Nomination Period ends, upon Lilly's election and payment of an extension fee. Under the terms of the Lilly Agreement, Lilly received 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 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 (the "Lilly Share Purchase

Agreement"). We 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, 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.

iECURE

In August 2021, we entered into a development and license agreement with iECURE under which iECURE was to advance our PBGENE-PCSK9 candidate through preclinical activities as well as a Phase 1 clinical trial as partial consideration for a license to our PCSK9-directed ARCUS nuclease to develop gene-insertion therapies for four other rare genetic diseases, including OTC deficiency, Citrullinemia Type 1, PKU, and another program focused on liver disease (the "iECURE Agreement"). We have made the decision to cease pursuit of PBGENE-PCSK9 for FH with iECURE as our partner. PGENE-PCSK9 for FH remains wholly-owned by us.

Simultaneously with the entry into the iECURE Agreement, we entered into an Equity Issuance Agreement with iECURE, pursuant to which iECURE issued us common stock in iECURE as additional consideration for the license to use our PCSK9-directed ARCUS nuclease.

Servier

In February 2016, we entered into the Servier Agreement with Servier, pursuant to which we agreed to develop allogeneic CAR T cell therapies for five unique antigen targets. One target was selected at the Servier 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. Upon selection of an antigen target under the Servier Agreement, we 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.

On April 9, 2021, we entered into the Program Purchase Agreement with Servier, pursuant to which we reacquired all of our global development and commercialization rights previously granted to Servier pursuant to the Servier Agreement, and mutually terminated the Servier Agreement.

Pursuant to the Servier Agreement, we had developed certain allogeneic CAR T candidates, including azer-cel and the stealth cell PBCAR19B, each targeting CD19, as well as four additional product targets ("Servier Targets"). Pursuant to the Program Purchase Agreement, we regained full global rights to research, develop, manufacture and commercialize products resulting from such programs, with sole control over all activities. Additionally, per the terms of the Program Purchase Agreement we do not have an obligation to continue development of the Servier Targets. With respect to products directed to CD19, Servier has certain rights of negotiation, which may be exercised during a specified time period if we elect to initiate a process or entertain third party offers for partnering such products.

Pursuant to the terms of the Program Purchase Agreement, we made a payment of $1.25 million in cash to Servier and agreed to waive earned milestones totaling $18.75 million that would have been otherwise payable to us.

The Program Purchase Agreement also requires us to make certain payments to Servier based on the achievement of regulatory and commercial milestones for each product, and a low- to mid-single-digit percentage royalty (subject to certain reductions) based on net sales of approved products, if any, resulting from any continued development and commercialization of the programs by us, for a period not to exceed ten years after first commercial sale of the applicable product in the United States or certain countries in Europe. If we enter into specified product partnering transactions, the Program Purchase Agreement requires us to pay to Servier a portion of certain consideration received pursuant to such product partnering transactions in lieu of the foregoing milestones (with the exception of a one-time clinical phase development milestone) and royalties. For additional discussion of accounting for payment obligations arising from the Program Purchase Agreement, refer to Note 6, *Commitments and Contingencies* to our consolidated financial statements included elsewhere in this Annual Report on Form 10-K (the "Financial Statements")

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 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 foreign 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 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.

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.

Tiziana

In September 2021, we entered into an exclusive license agreement to evaluate Tiziana's foralumab, a fully human anti-CD3 monoclonal antibody, as a lymphodepleting agent in conjunction with our allogeneic CAR T cells for the potential treatment of cancers. We plan to assess foralumab use in combination with an allogeneic CAR T.

SpringWorks Therapeutics

In September 2020, we entered into a Clinical Trial Collaboration Agreement with SpringWorks Therapeutics, Inc. Pursuant to such agreement, PBCAR269A was evaluated in combination with nirogacestat, SpringWorks' investigational GSI, in patients with R/R multiple myeloma. Under the terms of the agreement, we were responsible for all costs associated with the conduct of the clinical trial including providing PBCAR269A for use in the trial, and SpringWorks was responsible for providing nirogacestat at its sole cost and expense. The combination therapy and increased dose of PBCAR269A resulted in improved cell expansion, which correlated with increased clinical activity when compared to dose-matched PBCAR269A monotherapy treatment. However, in light of the competitive landscape of BCMA targeted therapies in multiple myeloma, we have made the strategic decision not to continue the PBCAR269A clinical program.

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. In April 2020, both parties agreed to coordinate a wind-down of all activities in their entirety under the agreement, effective as of June 2020, however, in August 2020 and subsequently in January 2021, both parties agreed to extend certain portions of the agreement through 2024. We will not be required to make termination payments to Penn.

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, 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 and pharmaceutical 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 sector, including companies such as Allogene Therapeutics, Inc., Alnylam Pharmaceuticals, Inc., Beam Therapeutics, Inc., Bristol-Myers Squibb Company, Caribou Biosciences, Inc., Cellectis S.A., CRISPR Therapeutics, AG, Editas Medicine, Inc., Intellia Therapeutics, Inc., Moderna, Inc., Prime Medicine, Inc., and Verve 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. Gilead Sciences, Inc., and Bristol-Myers Squibb Company have obtained FDA approval for autologous immunotherapies, and a number of companies, including Cellectis S.A., Allogene Therapeutics, Poseida Therapeutics and CRISPR Therapeutics AG, are pursuing allogeneic immunotherapies. 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.

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 and *in vivo* gene editing 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, 2022, we have an exclusive license from Duke under 12 issued U.S. patents and two pending U.S. patent applications. In addition, as of December 31, 2022, we own 37 issued U.S. patents, 38 pending non-provisional U.S. patent applications, and 19 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 will 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 pending patent applications in each of the United States, Europe, Australia, and two pending applications in Japan. 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 will 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 pending patent applications in each of the United States and 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 will have a standard expiration date of July 14, 2029, subject to potential extensions.

The fourth family, which we own, includes pending patent applications in each of the United States, Europe, Hong Kong, Australia, Canada, China, Israel, Japan, South Korea, and Mexico. 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 22 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 ten issued U.S. patents, two issued patents in each of Europe and Israel, one issued patent in each of Australia, Hong Kong, and Japan, pending patent applications in each of Europe, Australia, Canada, China, Hong Kong, Mexico, and South Korea, and two pending patent applications in each of the United States, Japan, and Israel. 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 will have a standard expiration date of October 5, 2036, subject to potential extensions.

The second family includes two issued patents in each of the United States and Europe, one issued patent in Australia, Hong Kong, and Japan, and pending patent applications in each of the United States, Europe, Australia, Canada, and Japan. 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 pending patent applications in each of the United States, Europe, Australia, Canada, China, Hong Kong, 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 have a standard expiration date of April 11, 2039, subject to potential extensions.

The fourth family includes two issued patents in each of the United States and Europe, one issued patent in each of Australia, Hong Kong, and Japan, pending patent applications in each of the United States, Europe, Australia, Canada, and Hong Kong, and two pending patent applications in Japan. 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 will have a standard expiration date of October 4, 2037, subject to potential extensions.

The fifth family includes one pending patent application in the United States. The patent application in this family includes 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 one issued patent in each of Europe and Japan, pending patent applications in each of the United States, Europe, Australia, and Canada, and two pending patent applications in Japan. Patent applications in this family include claims directed to (1) recombinant meganucleases that recognize and cleave a recognition sequence within the human β2m 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 β2m, (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 will have a standard expiration date of December 22, 2036, subject to potential extensions.

The seventh family includes one issued patent in each of the United States and Japan, and pending patent applications in each of 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 β2m 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 β2m 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 will have a standard expiration date of May 8, 2038, subject to potential extensions.

The eighth family includes one issued patent in the United States, pending patent applications in each of the United States, Europe, Australia, Canada, and Hong Kong, and two pending patent applications in 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 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 have a standard expiration date of October 3, 2038, subject to potential extensions.

The tenth family includes pending patent applications in each of the United States, Europe, and Canada. 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 four issued patents in the United States, one issued patent in China, pending patent applications in each of the United States, Europe, Australia, Canada, China, Hong Kong, Japan, Mexico, and South Korea, and two pending patent applications in Israel. 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 will have a standard expiration date of April 3, 2040, subject to potential extensions.

The twelfth family includes pending patent applications in each of the United States, Europe, Australia, Canada, Japan, and Hong Kong. Patent applications in this family include claims directed to methods of immunotherapy comprising administering to a subject a CD3 antibody, or antigen binding fragment thereof, that binds CD3 for the purpose of lymphodepletion, in combination with the administration of genetically-modified T cells that do not have detectable CD3 expression on the cell surface. Patents in this family, if issued, will have a standard expiration date of August 20, 2040, subject to potential extensions.

The thirteenth family includes a pending patent application in the United States. Patent applications in this family include claims directed to (1) polynucleotides encoding a CD20-specific chimeric antigen receptor, (2) methods of producing a genetically-modified T cell comprising such polynucleotides, (3) a genetically-modified T cell comprising such polynucleotides, (4) populations of such genetically-modified T cells, (5) pharmaceutical compositions comprising such genetically-modified T cells or populations, and (6) methods of immunotherapy for treating cancer in a subject. Patents in this family, if issued, will have a standard expiration date of October 30, 2040, subject to potential extensions.

The fourteenth family includes a pending patent applications in each of the United States, Europe, and Canada. Patent applications in this family include claims directed to a method of immunotherapy for treating cancer in a subject. Patents in this family, if issued, will have a standard expiration date of December 3, 2040, subject to potential extensions.

The fifteenth family includes a pending PCT international patent application and a pending patent application in the United States. Patent applications in this family include claims directed to methods for reducing the number of target cells, such as cancer cells, in a subject. Patents in this family, if issued, will have a standard expiration date of May 14, 2041, subject to potential extensions.

The sixteenth family includes a pending PCT international patent application and a pending patent application in the United States. Patent applications in this family include claims directed to a method for reducing the number of target cells, such as cancer cells, in a subject. Patents in this family, if issued, will have a standard expiration date of May 14, 2041, subject to potential extensions.

The seventeenth family includes a pending PCT international patent application. Patent applications in this family include claims directed to (1) an isolated antibody, or antigen-binding fragment thereof, that specifically binds to BCMA, (2) a pharmaceutical composition comprising such an antibody, (3) a polynucleotide encoding such an antibody, and an expression vector comprising the same, (5) a method of treating cancer in a subject, (6) a polynucleotide comprising a nucleic acid sequence encoding a chimeric antigen receptor having an anti-BCMA binding domain, (7) a genetically-modified eukaryotic cell comprising such a polynucleotide, (8) a method for producing such a genetically-modified eukaryotic cell, (9) a population of such genetically-modified eukaryotic cells, (10) a pharmaceutical composition comprising such a population, and (11) a method for treating cancer in a subject. Patents in this family, if issued, will have a standard expiration date of August 10, 2041, subject to potential extensions.

The eighteenth family includes a pending PCT international patent application. Patent applications in this family include claims directed to (1) a lipid nanoparticle composition, (2) a method for transfecting a population of eukaryotic cells, (3) a method for introducing a nucleic acid into a population of eukaryotic cells, (4) a population of such eukaryotic cells, (5) a pharmaceutical composition comprising such a population, and (6) a method for reducing the number of target cells in a subject. Patents in this family, if issued, will have a standard expiration date of October 6, 2041, subject to potential extensions.

The nineteenth family includes a pending PCT international patent application. Patent applications in this family include claims directed to (1) a genetically-modified eukaryotic cell comprising a nucleic acid sequence encoding a TGFB-1 inhibitory agent and a nucleic acid sequence encoding an engineered antigen receptor, (2) a genetically-modified eukaryotic cell comprising an inactivated TGFB-1 gene and a nucleic acid sequence encoding an engineered antigen receptor, (3) methods of producing such genetically-modified eukaryotic cells, (4) populations of such genetically-modified eukaryotic cells, (5) pharmaceutical compositions comprising such genetically-modified eukaryotic cells, and (6) methods for reducing the number of target cells in a subject comprising administering such populations of genetically-modified eukaryotic cells. Patents in this family, if issued, will have a standard expiration date of January 28, 2042, subject to potential extensions.

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

Other Patent Families

We own three patent families directed to gene therapy for HBV. The first family includes three issued patents in the United States, two issued patents in Japan, one issued patent in South Korea, pending patent applications in the United States, Europe, Australia, Canada, China, Guatemala, Israel, Japan, South Korea, Mexico, Morocco, the Philippines, Saudi Arabia, and Thailand, and two pending patent applications in each of Eurasia and Hong Kong. Patents in this family have a standard expiration date of October 13, 2037, subject to potential extensions. The second family includes one issued patent in the United States, and pending patent applications in the United States, Europe, and the Gulf Cooperation Council. Patents in this family will have a standard expiration date of April 11, 2039, or April 12, 2039, subject to potential extensions. The third family includes pending patent applications in each of the United States, Europe, China, and New Zealand. 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 each of the United States, Europe, Australia, Canada, China, Hong Kong, Israel, Mexico, and South Korea, and two pending patent applications in Japan. 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 each of the United States and Japan, one issued patent in Australia, and pending patent applications in each of the United States, Europe, Australia, Canada, and Japan. Patents in this family will have a standard expiration date of September 8, 2036, subject to potential extensions. The second family includes a pending PCT international patent application and pending patent applications in each of the United States, Europe, and Canada. Patents in this family, if issued, will have a standard expiration date of May 11, 2041, subject to potential extensions.

We own two patent families that are directed to engineered meganucleases and methods of treatment targeting the hydroxyacid oxidase 1 gene, which is associated with primary hyperoxaluria 1. The first family includes pending patent applications in the United States and Europe. Patents in this family, if issued, will have a standard expiration date of December 20, 2039, subject to potential extensions. The second family includes a pending PCT international patent application and a pending patent application in Canada. Patents in this family, if issued, will have a standard expiration date of January 7, 2042, 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 one issued patent in each of the United States and Europe, and pending patent applications in the United States, Europe, Australia, Canada, and Japan. Patents in this family 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 September 27, 2043, 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 PCT international patent application and a pending patent application in Canada. Patents in this family, if issued, will have a standard expiration date of August 20, 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 one issued patent in each of Europe and Japan, pending patent applications in each of the United States, Europe, Australia, Hong Kong, and Canada, and two pending patent applications in Japan. Patents in this family will have a standard expiration date of March 12, 2035, subject to potential extensions. The second family includes a pending PCT international patent application and pending patent applications in each of the United States and Canada. Patent applications in this family, if issued, will have a standard expiration date of November 12, 2041.

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

We own one patent family directed to engineered meganucleases and methods of treating alpha-1 antitrypsin deficiency. This family includes two pending PCT international patent applications. Patents in this family, if issued, will have a standard expiration date of October 19, 2042.

We own one patent family directed to optimized polynucleotides for protein expression. This 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 January 7, 2043.

We own one patent family directed to engineered meganucleases that target mitochondrial genomes and methods of treating mitochondrial disorders. This family includes two pending provisional patent applications in the United States. Patents in this family, if issued, will likely have a standard expiration date of March 9, 2043, or August 23, 2043.

We jointly own one patent family directed to engineered meganucleases that target mitochondrial genomes and methods of treating mitochondrial disorders. This family includes two pending provisional patent applications in the United States, two pending PCT

international patent applications, and two pending applications in Canada. Patents in this family, if issued, will have a standard expiration date of April 22, 2042, or August 23, 2043.

We jointly own one patent family directed to methods for generating male sterile plants. This family includes one pending PCT international patent application. Patents in this family, if issued, will have a standard expiration date of April 22, 2042.

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 one pending patent application 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 pending patent applications 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 one issued patent in each of the United States and Europe, a pending patent application in Europe, and two pending patent applications in the United States. Patents in this family will have a standard expiration date of June 20, 2036, subject to potential extensions. The second family includes one pending PCT international patent application and one pending patent application in the United States. Patents in this family, if issued, will have a standard expiration date of May 10, 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 pending patent applications in each of the United States and Europe. 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 pending patent applications in each of the United States and Europe. Patents in this family, if issued, will have a standard expiration date of January 10, 2040, subject to potential extensions.
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.

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 United States Patent and Trademark Office (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 Biologics License Application ("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 trademark portfolio currently contains two registered trademarks in the United States, including ARCUS and ARC NUCLEASE. We also own registered trademarks for both ARCUS and ARC NUCLEASE in Europe, China, and Australia, and a registered

trademark for ARCUS in Canada. Additionally, we own pending trademark applications for Precision BioSciences and the Precision BioSciences logo in the United States, Europe, Australia, Canada, China, Japan, and the United Kingdom ("UK"), and pending trademark applications for Evade, PBStealth, StealthCAR, and StealthCAR T in the United States.

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 seven issued patents in each of the United States, Europe, and Australia, and one issued patent in each of Canada and 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 and other applicable regulations;
- demonstration of successful, reproducible manufacture of clinical trial material produced in compliance with 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 potential 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 to establish the safety, purity, potency, or effectiveness 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 potential FDA inspection of selected clinical investigation sites to assess compliance with Good Clinical Practices ("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. While the IND is active, progress reports summarizing the results of the clinical trials and nonclinical studies performed since the last progress report, among other information, must be submitted at least annually to the FDA, and written IND safety reports must be submitted to the FDA and investigators for serious and unexpected suspected adverse events, findings from other studies suggesting a significant risk to humans exposed to the drug, findings from animal or *in vitro* testing suggesting a significant risk to humans exposed to the drug, and any clinically important increased rate of a serious suspected adverse reaction compared to that listed in the protocol or investigator brochure.

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 review of 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.

Development of new treatments for cancer and genetic diseases often combine phase 1 and phase 2 trials as the treatment is studied in limited patient population with the specified disease. 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, potency, 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.

Within 60 days following submission of the application, the FDA reviews all NDAs and BLAs submitted to ensure that they are sufficiently complete for substantive review before it accepts them for filing. The FDA may request additional information rather than accept an NDA or BLA for filing. In this event, the NDA or BLA must be resubmitted with the additional information. The resubmitted application also is subject to review before the FDA accepts it for filing. Once a BLA has been accepted for filing, the FDA begins an in-depth substantive review. 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'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 product candidates that, if approved, would represent 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 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. 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.

In addition, the Pediatric Research Equity Act ("PREA") requires a sponsor to conduct pediatric clinical trials for most biologics, for a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration. Under PREA, BLAs and supplements thereto must contain a pediatric assessment unless the sponsor has received a deferral or waiver. The required assessment must evaluate the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations and support dosing and administration for each pediatric subpopulation for which the product has been determined safe and effective. The sponsor or FDA may request a deferral of pediatric clinical trials for some or all of the pediatric subpopulations. A deferral may be granted for several reasons, including a finding that the biologic is ready for approval for use in adults before pediatric clinical trials are complete or that additional safety or effectiveness data needs to be collected before the pediatric clinical trials begin. The FDA must send a noncompliance letter to any sponsor that fails to submit the required assessment, keep a deferral current or fails to submit a request for approval of a pediatric formulation.

Expedited Development and Review Programs

A sponsor may seek approval of its product candidate under programs designed to expedite FDA's review and approval of biological products that meet certain criteria. Specifically, 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 candidate, 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.

A product candidate intended to treat a serious or life-threatening disease or condition may also be eligible for breakthrough therapy designation to expedite its development and review. A product candidate can receive breakthrough therapy designation if preliminary clinical evidence indicates that the product candidate, alone or in combination with one or more other drugs or biologics, 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 includes all of the fast track program features, as well as more intensive FDA interaction and guidance beginning as early as Phase 1 and an organizational commitment to expedite the development and review of the product candidate, including involvement of senior managers.

Any product candidate submitted to the FDA for approval, including a product candidate with a fast track designation or breakthrough therapy designation, may also be eligible for other types of FDA programs intended to expedite development and review, such as accelerated approval. Under the accelerated approval program, the FDA may approve a BLA on a determination that the biologic has

an effect on 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. As a condition of accelerated approval, the FDA generally requires that the sponsor approve, perform or complete confirmatory clinical trials to verify the biologic's clinical benefit in relationship to the surrogate endpoint or ultimate outcome in relationship to the predicted 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 on an expedited basis if, for example, the confirmatory trial fails to verify the predicted clinical benefit of the product or the sponsor fails to conduct such confirmatory trials in a timely manner.

The Regenerative Medicine Advanced Therapy ("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. Product candidates 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 disease or condition 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 disease or condition 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.

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 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 Biologics Price Competition and Innovation Act of 2009 (the "BPCIA"), which created an abbreviated approval pathway for biological products that are biosimilar to or interchangeable with an FDA-licensed reference biological product.

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.

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.

Foreign Regulation

To market any product outside of the United States, we would need to comply with numerous and varying regulatory requirements of other countries regarding safety and efficacy and governing, among other things, clinical trials, marketing authorization, manufacturing, commercial sales and distribution of our products. Because biologically sourced raw materials are subject to unique contamination risks, their use may be restricted in some countries.

Whether or not we obtain FDA approval of a product, we must obtain the requisite approvals from regulatory authorities in foreign countries prior to the commencement of clinical trials or marketing of the product in those countries. The requirements and process governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. Failure to comply with applicable foreign regulatory requirements, may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

Non-clinical studies and clinical trials

Similarly to the United States, the various phases of non-clinical and clinical research in the European Union, ("EU"), are subject to significant regulatory controls.

Non-clinical studies are performed to demonstrate the health or environmental safety of new biological substances. Non-clinical (pharmaco-toxicological) studies must be conducted in compliance with the principles of good laboratory practice ("GLP"), as set forth in EU Directive 2004/10/EC (unless otherwise justified for certain particular medicinal products – e.g., radio-pharmaceutical precursors for radio-labelling purposes). In particular, non-clinical studies, both *in vitro* and *in vivo*, must be planned, performed, monitored, recorded, reported and archived in accordance with the GLP principles, which define a set of rules and criteria for a quality system for the organizational process and the conditions for non-clinical studies. These GLP standards reflect the Organization for Economic Co-operation and Development requirements.

Clinical trials of medicinal products in the EU must be conducted in accordance with EU 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 ("ATMPs"). If the sponsor of the clinical trial is not established within the EU, it must appoint an entity within the EU 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.

The regulatory landscape related to clinical trials in the EU has been subject to recent changes. The EU Clinical Trials Regulation ("CTR"), which was adopted in April 2014 and repeals the EU Clinical Trials Directive, became applicable on January 31, 2022. Unlike directives, the CTR is directly applicable in all EU member states without the need for member states to further implement it into national law. The CTR notably harmonizes the assessment and supervision processes for clinical trials throughout the EU via a Clinical Trials Information System, which contains a centralized EU portal and database.

While the Clinical Trials Directive required a separate CTA to be submitted in each member state in which the clinical trial takes place, to both the competent national health authority and an independent ethics committee, much like the FDA and IRB respectively, the CTR introduces a centralized process and only requires the submission of a single application for multi-center trials. The CTR allows sponsors to make a single submission to both the competent authority and an ethics committee in each member state, leading to a single decision per member state. The 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. The assessment procedure of the CTA has been harmonized as well, including a joint assessment by all member states concerned, and a separate assessment by each member state with respect to specific requirements related to its own territory, including ethics rules. Each member state's decision is communicated to the sponsor via the centralized EU portal. Once the CTA is approved, clinical study development may proceed.

The CTR foresees a three-year transition period. The extent to which ongoing and new clinical trials will be governed by the CTR varies. Clinical trials for which an application was submitted (i) prior to January 31, 2022 under the Clinical Trials Directive, or (ii) between January 31, 2022 and January 31, 2023 and for which the sponsor has opted for the application of the EU Clinical Trials Directive remain governed by said Directive until January 31, 2025. After this date, all clinical trials (including those which are ongoing) will become subject to the provisions of the CTR. Compliance with the CTR requirements by us and our third-party service providers, such as CROs, may impact our developments plans.

Medicines used in clinical trials must be manufactured in accordance with Good Manufacturing Practice ("GMP"). Other national and EU-wide regulatory requirements may also apply.

Marketing authorization

To market a medicinal product in the EU, we must obtain a marketing authorization ("MA"). To obtain regulatory approval of a product candidate under EU regulatory systems, we must submit a MA application ("MAA"). The process for doing this depends, among other things, on the nature of the medicinal product. There are two types of MAs:

- "Centralized MAs" are 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 are valid throughout the EU. The centralized procedure is mandatory for certain types of products, such as (i) medicinal products derived from biotechnology processes, (ii) designated orphan medicinal products, (iii) ATMPs (such as gene therapy, somatic cell therapy and tissue engineered products), and (iv) medicinal products containing a new active substance indicated for the treatment certain diseases, such as HIV/AIDS, cancer, neurodegenerative disorders, diabetes, auto immune and other immune dysfunctions and viral diseases. The centralized procedure is optional for products containing a new active substance not yet authorized in the EU, or for products that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the EU. Under the centralized procedure, the maximum timeframe for the evaluation of an MAA 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.
- "Conditional MAs" may be granted in cases where all the required safety and efficacy data are not yet available. The conditional MA is subject to conditions to be fulfilled for generating the missing data or ensuring increased safety measures. It is valid for one year and has to be renewed annually until fulfillment of all the conditions. Once the pending studies are provided, it can become a "standard" MA. However, if the conditions are not fulfilled within the timeframe set by the EMA, the MA ceases to be renewed. Furthermore, MAs may also be granted "under exceptional circumstances" when the applicant can show that it is unable to provide comprehensive data on the efficacy and safety under normal conditions of use even after the product has been authorized and subject to specific procedures being introduced. This may arise in particular when the intended indications are very rare and, in the present state of scientific knowledge, it is not possible to provide comprehensive information, or when generating data may be contrary to generally accepted ethical principles. This MA is close to the conditional MA as it is reserved to medicinal products to be approved for severe diseases or unmet medical needs and the applicant does not hold the complete data set legally required for the grant of a MA. However, unlike the conditional MA, the applicant does not have to provide the missing data and will never have to. Although the MA "under exceptional circumstances" is granted definitively, the risk-benefit balance of the medicinal product is reviewed annually and the MA is withdrawn in case the risk-benefit ratio is no longer favorable.
- "National MAs", are issued by the competent authorities of EU member states and only cover their respective territory, and are available for products not falling within the mandatory scope of the centralized procedure. Where a product has already been authorized for marketing in an EU member state, 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 EU member states 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. Product developers that benefit from PRIME designation can expect to be eligible for accelerated assessment but this is not guaranteed. Many benefits accrue to sponsors of product candidates with PRIME designation, including but not limited to, early and proactive regulatory dialogue with the EMA, frequent discussions on clinical trial designs and other development program elements, and accelerated MAA assessment once a dossier has been submitted. Importantly, a dedicated contact and rapporteur from the CHMP is appointed early in the PRIME scheme facilitating increased understanding of the product at EMA's committee level. An initial meeting initiates these relationships and includes a team of multidisciplinary experts at the EMA to provide guidance on the overall development and regulatory strategies. 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 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 EU, new products authorized for marketing, or reference products, generally receive eight years of data exclusivity and an additional two years of market exclusivity upon MA. 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 MA 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 MA 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.

There is a special regime for biosimilars, or biological medicinal products that are similar to a reference medicinal product but that do not meet the definition of a generic medicinal product, for example, because of differences in raw materials or manufacturing processes. For such products, the results of appropriate preclinical or clinical trials must be provided, and guidelines from the EMA detail the type of quantity of supplementary data to be provided for different types of biological product. There are no such guidelines for complex biological products, such as gene or cell therapy medicinal products, and so it is unlikely that biosimilars of those products will currently be approved in the EU. However, guidance from the EMA states that they will be considered in the future in light of the scientific knowledge and regulatory experience gained at the time.

Pediatric development

In the EU, MAAs for new medicinal products have to include the results of studies conducted in the pediatric population, in compliance with a pediatric investigation plan ("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 are 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 EU member states 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 Medicinal Products

In the EU, a medicinal product can be designated as an orphan 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 EU, an application for designation as an orphan product can be made any time prior to the filing of a MAA. Orphan designation entitles a party to incentives such fee reductions or fee waivers, protocol assistance, and access to the centralized procedure.

Upon grant of a MA, orphan medicinal products are entitled to a ten-year period of market exclusivity for the approved therapeutic indications, which means the competent authorities, cannot accept another application for a MA, or grant a MA, or accept an application to extend a MA for a similar medicinal product for the same indication for a period of ten years. The period of market exclusivity is extended by two years for orphan medicinal products that have also complied with an agreed PIP. No extension to any supplementary protection certificate can be granted on the basis of pediatric studies for orphan indications.

The orphan exclusivity 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 designation, for example because the product is sufficiently profitable not to justify market exclusivity, or where the prevalence of the condition has increased above the threshold. Granting of an authorization for another similar orphan medicinal product where another product has market exclusivity can happen at any time if: (i) the second applicant can establish that its product, although similar to the authorized product, is safer, more effective or otherwise clinically superior, (ii) inability of the applicant to supply sufficient quantities of the orphan medicinal product or (iii) where the applicant consents to a second orphan medicinal product application. A company may voluntarily remove a product from the orphan register.

Orphan designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

Post-Approval Requirements

Similar to the United States, both MA holders and manufacturers of medicinal products are subject to comprehensive regulatory oversight by the EMA, the European Commission and/or the competent regulatory authorities of the member states. The holder of a MA must establish and maintain a pharmacovigilance system and appoint an individual qualified person for pharmacovigilance ("QPPV") who is responsible for the establishment and maintenance of that system, and oversees the safety profiles of medicinal products and any emerging safety concerns. Key obligations include expedited reporting of suspected serious adverse reactions and submission of periodic safety update reports ("PSURs").

All new MAAs must include a risk management plan ("RMP") describing the risk management system that the company will put in place and documenting measures to prevent or minimize the risks associated with the product. The regulatory authorities may also impose specific obligations as a condition of the MA. Such risk-minimization measures or post-authorization obligations may include additional safety monitoring, more frequent submission of PSURs, or the conduct of additional clinical trials or post-authorization safety studies.

The advertising and promotion of medicinal products is also subject to laws concerning promotion of medicinal products, interactions with physicians, misleading and comparative advertising and unfair commercial practices. All advertising and promotional activities for the product must be consistent with the approved summary of product characteristics, and therefore all off-label promotion is prohibited. Direct-to-consumer advertising of prescription medicines is also prohibited in the EU. Although general requirements for advertising and promotion of medicinal products are established under EU directives, the details are governed by regulations in each member state and can differ from one country to another.

The aforementioned EU rules are generally applicable in the European Economic Area, or EEA, which consists of the 27 EU member states plus Norway, Liechtenstein and Iceland.

Failure to comply with EU and member state laws that apply to the conduct of clinical trials, manufacturing approval, MA of medicinal products and marketing of such products, both before and after grant of the MA, manufacturing of pharmaceutical products, statutory health insurance, bribery and anti-corruption or with other applicable regulatory requirements may result in administrative, civil or criminal penalties. These penalties could include delays or refusal to authorize the conduct of clinical trials, or to grant MA, product withdrawals and recalls, product seizures, suspension, withdrawal or variation of the MA, total or partial suspension of production, distribution, manufacturing or clinical trials, operating restrictions, injunctions, suspension of licenses, fines and criminal penalties.

Brexit and the Regulatory Framework in the United Kingdom

Since the end of the Brexit transition period on January 1, 2021, Great Britain ("GB") (England, Scotland and Wales) has not been directly subject to EU laws, however under the terms of the Ireland/Northern Ireland Protocol, EU laws generally apply to Northern Ireland. The EU laws that have been transposed into United Kingdom ("UK") law through secondary legislation remain applicable in GB. However, under the Retained EU Law (Revocation and Reform) Bill 2022, which is currently before the UK parliament, any retained EU law not expressly preserved and "assimilated" into domestic law or extended by ministerial regulations (to no later than June 23, 2026) will automatically expire and be revoked by December 31, 2023. However, new legislation such as the (EU) CTR is not applicable in GB.

The UK Medicines and Medical Devices Act 2021, has introduced delegated powers in favor of the Secretary of State or an 'appropriate authority' to amend or supplement existing regulations in the area of medicinal products and medical devices. This allows new rules to be introduced in the future by way of secondary legislation, which aims to allow flexibility in addressing regulatory gaps and future changes in the fields of human medicines, clinical trials and medical devices.

Since January 1, 2021, the Medicines and Healthcare products Regulatory Agency ("MHRA"), has been the UK's standalone medicines and medical devices regulator. As a result of the Northern Ireland protocol, different rules will apply in Northern Ireland than in GB; broadly, Northern Ireland will continue to follow the EU regulatory regime, but its national competent authority will remain the MHRA.

The MHRA has introduced changes to national licensing procedures, including procedures to prioritize access to new medicines that will benefit patients, including a 150-day assessment and a rolling review procedure. All existing EU MAs for centrally authorized products were automatically converted or grandfathered into UK MAs, effective in GB (only), free of charge on January 1, 2021, unless the MA holder chooses to opt-out. In order to use the centralized procedure to obtain a MA that will be valid throughout the EEA, companies must be established in the EEA. Therefore after Brexit, companies established in the UK can no longer use the EU centralized procedure and instead an EEA entity must hold any centralized MAs. In order to obtain a UK MA to commercialize products in the UK, an applicant must be established in the UK and must follow one of the UK national authorization procedures or one of the remaining post-Brexit international cooperation procedures to obtain an MA to commercialize products in the UK. The MHRA may rely on a decision taken by the European Commission on the approval of a new (centralized procedure) MA when determining an application for a GB authorization; or use the MHRA's decentralized or mutual recognition procedures which enable MAs approved in EU member states (or Iceland, Liechtenstein, Norway) to be granted in GB.

There will be no pre-MA orphan designation. Instead, the MHRA will review applications for orphan designation in parallel to the corresponding MA application. The criteria are essentially the same, but have been tailored for the market, i.e., the prevalence of the condition in GB, rather than the EU, must not be more than five in 10,000. Should an orphan designation be granted, the period or market exclusivity will be set from the date of first approval of the product in GB.

The UK regulatory framework in relation to clinical trials is derived from existing EU legislation (as implemented into UK law, through secondary legislation). On January 17, 2022, the MHRA launched an eight-week consultation on reframing the UK legislation for clinical trials. The consultation closed on March 14, 2022 and aims to streamline clinical trials approvals, enable innovation, enhance clinical trials transparency, enable greater risk proportionality, and promote patient and public involvement in clinical trials. The outcome of the consultation is being closely watched and will determine whether the UK chooses to align with the (EU) CTR or diverge from it to maintain regulatory flexibility.

Other 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 EU, 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 non-physician practitioners including physician assistants and nurse practitioners, 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 foreign 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 EU, 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 ACA, enacted in March 2010, has substantially changed healthcare financing and delivery by both governmental and private insurers. Among other things the ACA 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.

Since its enactment, there have been judicial, administrative, executive, and legislative challenges to certain aspects of the ACA. On June 17, 2021, the U.S. Supreme Court (the "Supreme Court") dismissed the most recent judicial challenge to the ACA brought by several states on procedural grounds without specifically ruling on the constitutionality of the ACA. Thus, the ACA will remain in effect in its current form. Prior to the Supreme Court's decision, President Biden issued an executive order that initiated a special enrollment period from February 15, 2021 through August 15, 2021 for purposes of obtaining health insurance coverage through the ACA marketplace. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. It is unclear how other health reform measures of the Biden administration will impact our business.

In addition, other legislative changes have been proposed and adopted since the ACA 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, 2022, unless additional Congressional action is taken. On August 16, 2022, President Biden signed the Inflation Reduction Act of 2022, or IRA, into law, which among other things, extends enhanced subsidies for individuals purchasing health insurance coverage in ACA marketplaces through plan year 2025. The IRA also eliminates the "donut hole" under the Medicare Part D program beginning in 2025 by significantly lowering the beneficiary maximum out-of-pocket cost and creating a new manufacturer discount program. It is possible that the ACA will be subject to judicial or Congressional challenges in the future. 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.

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. 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.

On December 13, 2021, Regulation No. 2021/2282 on Health Technology Assessment ("HTA") was adopted. While the Regulation entered into force in January 2022, it will only begin to apply from January 2025 onwards, with preparatory and implementation-related steps to take place in the interim. Once the Regulation becomes applicable, it will have a phased implementation depending on the concerned products. This regulation intends to boost cooperation among EU member states in assessing health technologies, including new medicinal products, and providing the basis for cooperation at the EU level for joint clinical assessments in these areas. The regulation will permit EU member states to use common HTA tools, methodologies, and procedures across the EU, working together in four main areas, including joint clinical assessment of the innovative health technologies with the most potential impact for patients, joint scientific consultations whereby developers can seek advice from HTA authorities, identification of emerging health technologies to identify promising technologies early, and continuing voluntary cooperation in other areas. Individual EU member states will continue to be responsible for assessing non-clinical (e.g., economic, social, ethical) aspects of health technology, and making decisions on pricing and reimbursement.

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, and consumer protection laws and regulations, 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 foreign laws, govern the privacy and security of personal information, including health-related information in certain circumstances, 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 cultivated a culture that values innovation, accountability, respect, adaptability and perseverance. We strive to create an open, collaborative workplace that empowers Precisioneers to be their authentic selves and deliver meaningful and inspiring work. We strongly believe that our shared values will empower our team to better navigate and overcome challenges we may experience as we pursue our mission of improving life through genome editing. Through our diverse hiring and talent development practices with a focus on inclusion, we have recruited and successfully retained world class talent with industry leading experience in genome editing. We will continue to build on these critical capabilities to successfully impact the patients we ultimately wish to serve. We believe that all Precisioneers are inspired by developing high quality research and have a passion to translate their work into therapies dedicated to improving life.

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 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, development of 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. As of February 21, 2023, our workforce was self-reportedly approximately 49% women and approximately 27% Asian, Black, Latinx, two or more races, or not defined. Our senior leadership team and department heads were self-reportedly approximately 31% women and 8% Asian or Black as of February 21, 2023.

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.

As of December 31, 2022, we had 198 full-time Precisioneers. Of these full-time employees, 156 are engaged in research and development activities and 40 have Ph.D. or M.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 not been profitable and may not achieve or maintain profitability.

We 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 loss was $111.6 million for the December 31, 2022. As of December 31, 2022, we had an accumulated deficit of $428.3 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 proceeds from upfront and milestone payments from collaboration and licensing agreements, our IPO, private placements of our common stock, convertible preferred stock and convertible debt financings, underwritten and at-the-market offerings of common stock, and borrowings on credit facilities. 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. We anticipate our expenses will increase if and as we:

- continue our current research and development programs, including conducting laboratory and preclinical studies for product candidates;
- continue to conduct or initiate clinical 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 new and retain 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. Even if a therapeutic product candidate receives regulatory approval, 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 studies and clinical 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 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, as of the date of this Annual Report on Form 10-K, existing cash and cash equivalents, continued operational discipline, and available credit will allow us to fund operating expense and capital expenditure requirements through the first quarter of 2025. 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 studies and clinical 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.

In May 2019, the Company entered into a loan and security agreement with Pacific Western Bank ("PWB") (as subsequently amended, the "Revolving Line"). Pursuant to the terms of the Revolving Line, we may request advances on a revolving line of credit of up to an aggregate principal of $30.0 million and the maturity date of the Revolving Line is June 23, 2024. As of December 31, 2022, we had $22.5 million in borrowings under our Revolving Line. Pursuant to the terms of the Revolving Line, 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 Revolving Line 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, including in underwritten and at-the-market offerings, stockholders' ownership interest will be diluted, and the terms of such securities may include liquidation or other preferences that adversely affect common stockholders' rights. 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 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 1b/2a clinical trial in patients with R/R NHL and R/R B-ALL and a Phase 1 clinical trial in patients with NHL. In addition, we will not be continuing a previously initiated Phase 1/2a clinical trial in patients with R/R multiple myeloma, in light of the competitive landscape of BCMA targeted therapies in multiple myeloma. We have not yet demonstrated an ability to successfully complete any clinical 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, particularly the nascent and swiftly evolving gene editing field, 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 industry 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 are continually evaluating our business strategy and may modify this strategy in light of developments in our business and other factors. 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 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, as part of the ongoing strategic prioritization exercise, in 2023 we announced that while we will continue to pursue gene knock-out opportunistically, the proof-of-concept data continues to lead toward prioritizing programs involving complex edits and gene insertion. As such, we made the decision to cease pursuit of PBGENE-PCSK9 for FH with iECURE as our partner. We also made the choice to look for a partner in the kidney disease arena for further development of PBGENE-PH1 and will no longer develop the program on our own. There is no guarantee that this ongoing prioritization review will ultimately lead to any viable commercial products, profitable market opportunities or other value-enhancing activities. 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.

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 three 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 studies and clinical trials. There have been a limited number of clinical trials of products created with genome editing technologies, four 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 of our product candidates in human trials. 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. Our product candidates may not be able to properly implement desired genetic edits with sufficient accuracy to be viable therapeutic 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 studies or any clinical 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 ("TALENs") and clustered regularly interspaced short palindromic repeats associated protein-9 nuclease ("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, 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 editing programs targeting HBV, DMD, and certain hemoglobinopathies, among other indications. 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 and CD19B product candidates, all of our product candidates and product development programs we are currently pursuing are still in the discovery or preclinical stages. We may be unsuccessful in advancing those product candidates into clinical development 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, the terms of our collaborative arrangements may change, or our collaborative arrangements may be terminated;
- 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 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, participation of third parties including outside collaborators or vendors, the receipt of key regulatory approvals or actions, and other factors, including without limitation, impacts resulting from the COVID-19 pandemic and its variants, 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. 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.

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, 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.

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 sector, including companies such as Allogene Therapeutics, Inc., Alnylam Pharmaceuticals, Inc., Beam Therapeutics Inc., Caribou Biosciences, Inc., Cellectis S.A., CRISPR Therapeutics AG, Editas Medicine, Inc., Intellia Therapeutics, Inc., and Verve Therapeutics, Inc. Several companies, including Novartis Pharmaceuticals Corp., Celgene Corp., and Gilead Sciences, Inc. have obtained FDA approval for autologous immunotherapies, and a number of companies, including Cellectis S.A., Allogene Therapeutics and CRISPR Therapeutics AG, are pursuing allogeneic immunotherapies. We expect that our operations focused on developing

products for *in vivo* gene editing 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.

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 testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products 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, 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 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, political instability in particular foreign economies and markets, or civil unrest or war, such as the current conflict between Russia and Ukraine;
- 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 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. 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 Therapeutic Products within its Center for Biologics Evaluation and Research ("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 ("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 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 EU. The EMA has a Committee for Advanced Therapies ("CAT") that is responsible for assessing the quality, safety and efficacy of ATMPs. ATMPs 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 foreign 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 submit INDs to the FDA or CTAs to comparable foreign authorities to commence additional clinical trials on the timelines we expect, and even if we are able to, the FDA or comparable foreign authorities may not permit us to proceed.

We plan to submit INDs and CTAs 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, CTA, 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 and *in vivo* therapies for genetic and infectious diseases remains an emerging and evolving field. Accordingly, we expect CMC related topics, including product specifications, will be a focus of IND and CTA reviews, which may delay receipt of authorization to proceed under

INDs and CTAs. Additionally, even if such regulatory authorities agree with the design and implementation of the clinical trials set forth in an IND or CTA, we cannot guarantee that such regulatory authorities will not change their requirements in the future. Similar risks may exist in foreign jurisdictions where we intend to conduct clinical trials.

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 impose similar requirements. The time required to obtain approval by the FDA 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 or foreign regulatory authorities. 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 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 our manufacturing processes or facilities or those of third-party manufacturers with which we or our collaborators contract for clinical and commercial supplies;
- the FDA, comparable foreign regulatory authorities or notified bodies may fail to approve or certify 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 REMS or similar risk management measures. 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.

In addition, FDA and foreign regulatory authorities may change their approval policies and new regulations may be enacted. For instance, the EU pharmaceutical legislation is currently undergoing a complete review process, in the context of the Pharmaceutical Strategy for Europe initiative, launched by the European Commission in November 2020. The European Commission's proposal for revision of several legislative instruments related to medicinal products (potentially revising the duration of regulatory exclusivity, eligibility for expedited pathways, etc.) is currently expected during the first quarter of 2023. The proposed revisions, once they are

agreed and adopted by the European Parliament and European Council (not expected before the end of 2024 or early 2025) may have a significant impact on the biopharmaceutical industry in the long term.

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 1b/2a clinical trial in patients with R/R NHL or R/R B-ALL, and a Phase 1 clinical trial in patients with NHL. In addition, we will not be continuing a previously initiated Phase 1/2a clinical trial in subjects with R/R multiple myeloma, in light of the competitive landscape of BCMA targeted therapies in 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 ("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 or ethics committee approval or positive opinion 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 ("DSMB") for such trial or by the FDA or other foreign 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;
- competitive pressures and other market conditions;
- 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 and its variants, 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.

If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies governing clinical trials, our development plans may also be impacted.

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, thawing 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 ("CMOs") as well as our dedicated manufacturing facility, MCAT. The facilities used by us and our contract manufacturers to manufacture therapeutic product candidates must be evaluated for the manufacture of our product candidates by the FDA or foreign regulatory authorities pursuant to inspections that will be conducted after we submit a BLA to the FDA, or similar foreign applications to foreign regulatory authorities. We do not control the manufacturing process of our contract manufacturers and are dependent on their compliance with cGMP or similar foreign requirements 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' GMP 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 MCAT, 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 and its variants 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 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 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 interim, initial or "top-line" data from preclinical studies or clinical trials, which is based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular trial. 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, initial and "top-line" 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, including large deletions and translocations or chromosomal abnormalities. 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. Such unintended and undesirable side effects were exhibited in one of our competitors' clinical trials for which a clinical hold was placed by the FDA in October 2021 following a report of a chromosomal abnormality. 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, in our Phase 1b/2a clinical trial of azer-cel, there have been patient deaths which have been assessed as possibly related to study treatment, as well as patient deaths without disease progression that, while deemed unrelated to study treatment, may lead to adverse public perception of CAR T cell therapy.

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 or foreign regulatory authorities could require us to adopt a REMS or similar risk management measures 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 similar risk management measures 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 foreign 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 ("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 non-physician practitioners such as physician assistants and nurse practitioners, and teaching hospitals, and requires applicable manufacturers and group purchasing organizations to report annually to the Centers for Medicare and Medicaid Services ("CMS"), ownership and investment interests held by the physicians described above and their immediate family members; and
- analogous state and foreign 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 foreign 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 foreign. 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 foreign 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 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 the Department of Health and Human Services ("HHS"), affected individuals and if the breach is large enough, the media. Most healthcare providers, including

research institutions from which we obtain patient health information, are subject to privacy and security regulations promulgated under HIPAA. While we do not believe that we are currently acting as a covered entity or business associate under HIPAA and thus are not directly regulated under HIPAA, any person may be prosecuted under HIPAA's criminal provisions either directly or under aiding-and-abetting or conspiracy principles. Consequently, depending on the facts and circumstances, we could face substantial criminal penalties if we knowingly receive individually identifiable health information from a HIPAA-covered healthcare provider or research institution that has not satisfied HIPAA's requirements for disclosure of individually identifiable health information

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. For example, California enacted the California Consumer Privacy Act of 2018 ("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 has increased the likelihood of and risks associated with data breach litigation. Further, the California Privacy Rights Act ("CPRA") generally went into effect on January 1, 2023, and significantly amends the CCPA. The CPRA imposes 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 also creates a new California data protection agency authorized to issue substantive regulations and could result in increased privacy and information security enforcement. Similar laws have passed in Virginia, Colorado, Connecticut and Utah, and have been proposed in other states and at the federal level, reflecting a trend toward more stringent privacy legislation in the United States. The enactment of such laws could have potentially conflicting requirements that would make compliance challenging. 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 European Union General Data Protection Regulation ("GDPR") went into effect in May 2018 and imposes strict requirements for processing the personal data of individuals within the European Economic Area ("EEA"). Companies that must comply with the GDPR face increased compliance obligations and risk, including more robust regulatory enforcement of data protection requirements, and potential fines for noncompliance of up to €20 million or 4% of the annual global revenues of the noncompliant company, whichever is greater. Since January 1, 2021 we have also been 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.

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 ("CJEU") invalidated the EU-US Privacy Shield Framework, also known as 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. In March 2022, the U.S. and EU announced a new regulatory regime intended to replace the invalidated regulations; however, this new EU-US Data Privacy Framework has not been implemented beyond an executive order signed by President Biden on October 7, 2022 on Enhancing Safeguards for Untied States Signals Intelligence Activities. European court and regulatory decisions subsequent to the CJEU decision of July 16, 2020 have taken a restrictive approach to international data transfers. Additionally, the EU adopted the EU Clinical Trials Regulation, which came into effect on January 31, 2022. This regulation imposes obligations on the use of data generated from clinical trials and enables European patients to have the opportunity to access information about clinical trials.

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 azer-cel for the treatment of ALL and MCL, 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 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 the disease or condition 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 disease or condition 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 a disease or condition broader than the orphan designated disease or condition 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 can be approved for the same condition. Even after an orphan drug is approved, the FDA can subsequently approve the same drug 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 from the European Commission after receiving the opinion of the EMA's Committee for Orphan Medicinal Products, under Article 3 of Regulation (EC) 141/2000. This applies to products (1) that are intended for a life-threatening or chronically debilitating condition; and (2) either (a) such condition affects not more than five in 10,000 persons in the EU when the application is made, or (b) the product, without the benefits derived from orphan status, would be unlikely to generate sufficient returns in the EU to justify the necessary investment, and (3) 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 designation entitles a party to financial incentives such as reduction of fees, fee waivers, specific regulatory assistance and scientific advice, and access to the centralized marketing authorization procedure. Upon grant of a MA and assuming the requirements for orphan designation are also met at the time the marketing authorization is granted, orphan medicinal products are entitled to 10 years of market exclusivity for the approved therapeutic indication, 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 complying with an agreed Pediatric Investigation Plan. 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 judged as sufficiently profitable not to justify maintenance of market exclusivity, or when the prevalence of the condition has increased above the orphan designation threshold. 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.

Post-Brexit, the United Kingdom has retained the EU Regulation which governs the designation of medicinal products as orphan drugs and which establishes incentives thereto (Regulation (EC) No. 141/2000) as part of UK law by virtue of the European Union (Withdrawal) Act 2018. However under the Retained EU Law (Revocation and Reform) Bill, which is currently before the UK Parliament, unless this legislation is expressly preserved and "assimilated" into domestic law or extended by ministerial regulations (to no later than June 23, 2026) it will automatically expire and be revoked by December 31, 2023. There is therefore uncertainty about the future regulations relating to orphan designation in Great Britain, and any future changes to the legal requirements could lead to greater regulatory complexity and increased costs to our business.

The MHRA is responsible for reviewing applications from companies for orphan designation at the time of a marketing authorization application. If a medicinal product has been designated orphan in the EU under Regulation (EC) 141/2000, a Great Britain orphan MAA can be made under regulation 50G of the Human Medicines Regulation 2012 (as amended). A UK-wide orphan MAA can only be considered in the absence of an active EU orphan designation.

If a UK-wide orphan marketing authorization is granted and the medicinal product subsequently receives EU orphan designation, the market authorization holder would need to submit a variation to change this to a Great Britain orphan MA
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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, or Regenerative Medicine Advanced Therapy ("RMAT") designation, 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 azer-cel for the treatment of B-ALL. We may continue to seek fast track designation and may also seek breakthrough therapy designation, 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, or biologic, in our case, 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 biologic eligible for more frequent interactions with FDA to discuss the development plan and clinical trial design. A BLA for a fast track product candidate may also be eligible for rolling review, where the FDA may consider for review sections of the BLA on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the BLA, the FDA agrees to accept sections of the BLA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the BLA. A BLA for a product candidate with fast track designation may also be eligible for 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 voluntary scheme provided by the EMA to enhance support for the development of medicines that target an unmet medical need and are expected to be of major public health interest, which provides incentives similar to the Breakthrough therapy designation in the United States. It is based on increased interaction and early dialogue with companies developing promising medicines, to optimize their product development plans and speed up their evaluation to help them 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 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 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 designations for our product candidates, or that we will obtain breakthrough therapy designation, RMAT designation or access to PRIME or ATMP classification for any of our product candidates. Fast track designation, breakthrough therapy designation, RMAT designation, and PRIME and ATMP classification 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 classification eligibility. Additionally, fast track designation, breakthrough therapy designation, RMAT designation and access to PRIME or ATMP classification can each be revoked if applicable regulatory authorities decide that the criteria for eligibility cease to be met as clinical data emerges.

Further, product developers that benefit from PRIME designation may be eligible for accelerated assessment (in 150 days instead of 210 days), which may be granted for medicinal products of major interest from a public health perspective or that target an unmet medical need, but this is not guaranteed. The competent regulatory authorities in the EU have broad discretion whether to grant such an accelerated assessment, and, even if such assessment is granted, we may not experience a faster development process, review or authorization compared to conventional procedures.

We have obtained a rare pediatric disease designation for azer-cel for the treatment of B-ALL, however, there is no guarantee that FDA approval of will result in issuance of a priority review voucher.

In 2012, Congress authorized the FDA to award priority review vouchers to sponsors of certain rare pediatric disease product applications. This program is designed to encourage development of new drug and biological products for prevention and treatment of certain rare pediatric diseases. Specifically, under this program, a sponsor who receives an approval for a drug or biologic for a "rare pediatric disease" that meets certain criteria may qualify for a voucher that can be redeemed to receive a priority review of a subsequent marketing application for a different product. The sponsor of a rare pediatric disease drug product receiving a priority review voucher may transfer (including by sale) the voucher to another sponsor. The voucher may be further transferred any number of times before the voucher is used, as long as the sponsor making the transfer has not yet submitted the application. The FDA may also revoke any priority review voucher if the rare pediatric disease drug for which the voucher was awarded is not marketed in the U.S. within one year following the date of approval.

We have obtained seek a rare pediatric disease designation for azer-cel for the treatment of B-ALL, however, there is no guarantee that we will be able to obtain a priority review voucher, even if azer-cel is approved by the FDA. For example, the FDA may determine that a BLA, even if ultimately approved, does not meet the eligibility criteria for a priority review voucher, including for the following reasons:

- the product no longer meets the definition of a rare pediatric disease;
- the product contains an active ingredient that has been previously approved in another marketing application;
- the application does not rely on clinical data derived from studies examining a pediatric population and dosages of the drug intended for that population;
- the application is approved for a different adult indication than the rare pediatric disease for which the product is designated.

Moreover, Congress included a sunset provision in the statute authorizing the rare pediatric disease priority review voucher program. Under the current statutory sunset provisions, after September 30, 2024, FDA may only award a voucher for an approved rare pediatric disease product application if the sponsor has rare pediatric disease designation for the product candidate, and that designation was granted by September 30, 2024. After September 30, 2026, FDA may not award any rare pediatric disease priority review vouchers.

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 foreign 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 ACA, was enacted in the United States. Among the provisions of the Affordable Care Act of importance to our product candidates, the ACA 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, administrative, executive, and legislative challenges to certain aspects of the ACA, and the most recent judicial challenge to the ACA brought before the Supreme Court was dismissed in June 2021 resulting in the ACA remaining in effect in its current form. Prior to the Supreme Court's decision. President Biden issued an executive order instructing certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. It is unclear how other health reform measures will impact our business.

In addition, other legislative changes have been proposed and adopted since the ACA was enacted. These changes include the American Rescue Plan Act of 2021, which eliminates the statutory Medicaid drug rebate cap, currently set at 100% of a drug's average manufacturer price, beginning January 1, 2024.

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. Most recently, on August 16, 2022, the Inflation Reduction Act of 2022 (the "IRA"), was signed into law. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare (beginning in 2026), with prices that can be negotiated subject to a cap; imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation (first due in 2023); and replaces the Part D coverage gap discount program with a new discounting program (beginning in 2025). The IRA permits the Secretary of the HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years. For that and other reasons, it is currently unclear how the IRA will be effectuated. 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.

We expect that 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.

In the EU, similar developments may affect our ability to profitably commercialize our product candidates, if approved. In addition to continuing pressure on prices and cost containment measures, legislative developments at the EU or member state level may result in significant additional requirements or obstacles that may increase our operating costs. The delivery of healthcare in the EU, including the establishment and operation of health services and the pricing and reimbursement of medicines, is almost exclusively a matter for national, rather than EU, law and policy. National governments and health service providers have different priorities and approaches to the delivery of health care and the pricing and reimbursement of products in that context. In general, however, the healthcare budgetary constraints in most EU member states have resulted in restrictions on the pricing and reimbursement of medicines by relevant health service providers. Coupled with ever-increasing EU and national regulatory burdens on those wishing to develop and market products, this could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to commercialize our product candidates, if approved. In markets outside of the United States and EU, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies.

On December 13, 2021, Regulation No 2021/2282 on Health Technology Assessment (“HTA”) amending Directive 2011/24/EU, was adopted. While the Regulation entered into force in January 2022, it will only begin to apply from January 2025 onwards, with preparatory and implementation-related steps to take place in the interim. Once the Regulation becomes applicable, it will have a phased implementation depending on the concerned products. This regulation intends to boost cooperation among EU member states in assessing health technologies, including new medicinal products, and providing the basis for cooperation at the EU level for joint clinical assessments in these areas. The regulation will permit EU member states to use common HTA tools, methodologies, and procedures across the EU, working together in four main areas, including joint clinical assessment of the innovative health technologies with the most potential impact for patients, joint scientific consultations whereby developers can seek advice from HTA authorities, identification of emerging health technologies to identify promising technologies early, and continuing voluntary cooperation in other areas. Individual EU member states will continue to be responsible for assessing non-clinical (e.g., economic, social, ethical) aspects of health technology, and making decisions on pricing and reimbursement.

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 GMP 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 and foreign regulatory authorities strictly regulate 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 and foreign regulatory authorities 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. 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, we or they may be subject to enforcement action and we may not achieve or sustain profitability.

The FDA's and other regulatory authorities' policies with respect to clinical trials may change and additional government regulations may be enacted. For example, the FDA's Oncology Center of Excellence launched Project Optimus, an initiative to reform dose selection in oncology drug development, in 2021 and is still being implemented. If the FDA believes we have not sufficiently established that the selected dose or doses for our product candidates maximize efficacy as well as safety and tolerability, the FDA may require us to conduct additional clinical trials or generate additional dosing-related information, which could significantly delay and/or increase the expense of our clinical development programs.

It is currently unclear to what extent the United Kingdom ("UK") will seek to align its regulations with the EU. The UK regulatory framework in relation to clinical trials is derived from existing EU legislation (as implemented into UK law, through secondary legislation).

On January 17, 2022, the UK MHRA launched an eight-week consultation on reframing the UK legislation for clinical trials. The consultation closed on March 14, 2022 and aims to streamline clinical trials approvals, enable innovation, enhance clinical trials transparency, enable greater risk proportionality, and promote patient and public involvement in clinical trials. The outcome of the consultation is closely watched and will determine whether the UK chooses to align with the CTR or diverge from it to maintain regulatory flexibility. Under the terms of the Protocol on Ireland/Northern Ireland, provisions of the CTR which relate to the manufacture and import of investigational medicinal produces and auxiliary medicinal products apply in Northern Ireland. A decision by the UK Government not to closely align its regulations with the new approach that has been adopted in the EU may have an effect on the cost of conducting clinical trials in the UK as opposed to other countries.

The FDA and other regulatory agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses. If we are found or alleged to have improperly promoted off-label uses, we may become subject to significant liability.

The FDA and other regulatory agencies strictly regulate the promotional claims that may be made about prescription products, as our product candidates would be, if approved. In particular, a product may not be promoted for uses that are not approved by the FDA or such other regulatory agencies as reflected in the product's approved labeling. If we are found to have promoted such off-label uses, we may become subject to significant liability. The federal government has levied large civil and criminal fines against companies for alleged improper promotion and has enjoined several companies from engaging in off-label promotion. The FDA has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed. If we cannot successfully manage the promotion and avoid off-label promotion of our product candidates, if approved, we could become subject to significant liability, which would materially adversely affect our business and financial condition.

Disruptions at the FDA and other government agencies caused by funding shortages or global health concerns could hinder their ability to hire, retain or deploy key leadership and other personnel, or otherwise prevent new or modified products from being developed, approved or commercialized in a timely manner or at all, which could negatively impact our business.

The ability of the FDA and foreign regulatory authorities to review and approve new products can be affected by a variety of factors, including government budget and funding levels, statutory, regulatory and policy changes, the FDA's or foreign regulatory authorities' ability to hire and retain key personnel and accept the payment of user fees, and other events that may otherwise affect the FDA's or foreign regulatory authorities' ability to perform routine functions. Average review times at the FDA and foreign regulatory authorities have fluctuated in recent years as a result. In addition, government funding of other government agencies that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable. Disruptions at the FDA and other agencies, such as the EMA following its relocation to Amsterdam and resulting staff changes, may also slow the time necessary for new biologics or modifications to approved biologics to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical FDA employees and stop critical activities.

Separately, in response to the COVID-19 pandemic, the FDA postponed most inspections of domestic and foreign manufacturing facilities at various points. Even though the FDA has since resumed standard inspection operations of domestic facilities where feasible, the FDA has continued to monitor and implement changes to its inspectional activities to ensure the safety of its employees and those of the firms it regulates as it adapts to the evolving COVID-19 pandemic, and any resurgence of the virus or emergence of new variants may lead to further inspectional delays Regulatory authorities outside the United States have adopted similar restrictions or other policy measures in response to the COVID-19 pandemic and its variants. If a prolonged government shutdown occurs, or if global health concerns continue to prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews or other regulatory activities, it could significantly impact the ability of the FDA or other regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

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 or other regulatory authorities;
- product labeling or product insert requirements of the FDA 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, as a company, 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 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.

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. 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.

Jurisdictions in addition to the U.S. have established abbreviated pathways for regulatory approval of biological products that are biosimilar to earlier approved reference products. For example, the EU has had an established regulatory pathway for biosimilars since 2006.

Risks Related to Our Organization, Structure and Operations

We may experience difficulties in managing our growth, which could disrupt our operations.

As of December 31, 2022, we had 198 full-time employees. 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, or 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 key executives, as well as attracting, retaining and motivating 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. 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 new or successor 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, (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 (“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 (“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 may suffer in the event of information technology system failures, cyber-attacks or deficiencies in our security, which could materially affect our results.

Despite the implementation of security measures, our information technology systems, as well as those of third parties with which we have relationships, are vulnerable to attack, interruption, and damage from computer viruses and malware (e.g., ransomware), malicious code, cyberattacks, hacking, phishing attacks and other social engineering schemes, denial or degradation of service attacks, natural and manmade disasters, terrorism, war and telecommunication and electrical failures, malfeasance by external or internal parties (e.g., employee theft or misuse, attacks by sophisticated nation-state and nation-state-supported actors), and human error. The aforementioned third parties with which we have relationships include service providers and vendors who provide to us a broad array of software and other technologies as well as products, services and functions (e.g., human resources, finance, communications, data transmission, risk, compliance) that enable us to conduct, monitor and/or protect our business, operations, systems and data assets.

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. Furthermore, because the technologies used to obtain unauthorized access to, or to sabotage or disrupt, 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. Even if identified, we may be unable to adequately investigate or remediate incidents or breaches due to attackers increasingly using tools and techniques that are designed to circumvent controls, to avoid detection, and to remove or obfuscate forensic evidence. As a result of the COVID-19 pandemic and the continued hybrid work environment, we may also face increased cybersecurity risks due to our reliance on internet technology and the number of our and our service providers' employees who are (and may continue to be) working remotely, which may create additional opportunities for cybercriminals to exploit vulnerabilities. The White House, SEC and other regulators have also increased their focus on companies' cybersecurity vulnerabilities and risks.

We and certain of our service providers are from time to time, subject to cyberattacks and security incidents. While we do not believe that we have experienced any significant system failure, accident or security breach to date, if such an event were to occur and cause interruptions in our or our critical third parties' operations, it could result in delays and/or material disruptions of our research and development programs, our operations and ultimately, our financial results. 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 due to delays in the development of our product candidates and/or due to reputational harm, litigation, regulatory investigations and enforcement, fines and penalties, or increased costs of compliance and system remediation. Any losses, costs or liabilities may not be covered by, or may exceed the coverage limits of, any or all applicable insurance policies.

Federal, state and foreign legislators and regulators globally have enacted or proposed legal requirements regarding the collection, distribution, disclosure, use, processing, security and storage of personally identifiable information and other types of regulated data, including online information and data online. 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 security measures that we and our critical third parties (e.g., collaborators) implement, our information technology systems, infrastructure and data may be vulnerable to attacks by hackers or internal bad actors, breaches due to human 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 and other parties of security breaches involving particular types of 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 relationships that involve the handling or processing of such information.

Even though we may have contractual protections with third parties who process or handle sensitive information, any 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, may 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 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. We may operate in foreign jurisdictions in the future. We could become subject to income and non-income taxes in foreign 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 ("IRS") or other taxing authorities may disagree with our positions. If the IRS 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 not achieve profitability. As of December 31, 2022, we had U.S. federal and state net operating loss ("NOL") carryforwards of $159.5 million and $119.1 million, respectively. Our federal NOL carryforwards carry forward indefinitely. The state NOL carryforwards begin to expire in 2027. In addition, as of December 31, 2022, we have U.S. federal and state research and development ("R&D") tax credits of $13.2 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, 2022 and December 31, 2021, we had federal Orphan Drug credits of $11.6 million and $9.5 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 NOL carryforwards. For example, legislation enacted in 2017, informally titled the Tax Cuts and Jobs Act (the "TCJA"), significantly revised the Internal Revenue Code of 1986, as amended. Future guidance from the IRS and other tax authorities with respect to the TCJA may affect us, and certain aspects of the TCJA could be repealed or modified in future legislation. For example, the Coronavirus Aid, Relief, and Economic Security Act (the "CARES Act") modified certain provisions of the TCJA. Under the CARES Act, NOLs 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 TCJA, 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 NOLs 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 TCJA or the CARES Act.

As of December 31, 2022, 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 Internal Revenue Code of 1986, as amended, limit a corporation's ability to utilize its NOL 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 NOL 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 NOL carryforwards (and research tax credits) may expire prior to being used, and our NOL 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.

COVID-19 has impacted, and may continue to impact, 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.

The COVID-19 pandemic and government measures taken in response have had a significant impact, both direct and indirect, on businesses and commerce, as at various points during the pandemic, worker shortages have occurred; supply chains and manufacturing, including our own, 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 has fallen. Any additional resurgence of COVID-19, or any other pandemic, epidemic or outbreak of an infectious disease, along with any new regulatory orders or guidance or any self-imposed protective measures that we or our partners impose in response, could adversely impact our business, including our preclinical studies and clinical trials.

The COVID-19 pandemic and its variants continue to evolve. Disruptions, supply chain constraints and timeline impacts, staffing shortages, competing resource demands and safety concerns caused by the COVID-19 pandemic and its variants have caused, and may continue to cause, difficulties, disruptions or delays in conducting preclinical studies or initiating, enrolling, conducting or completing our planned and ongoing clinical trials and impact our ability to enroll patients, and we may incur other unforeseen costs as a result. Lead times for certain of our single-use components have been extended as a result of supply chain constraints affecting the industry, and global economic conditions could lead to even longer timelines or greater costs in the future. The extent to which the COVID-19 pandemic 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 emergence of additional new variants, business closures or business disruptions and the effectiveness of actions taken in the United States and other countries to contain and treat the disease. Additionally, the magnitude of the economic impact of COVID-19 pandemic and its variants including sustained inflation, supply chain disruptions, and major central bank policy actions continues to be difficult to assess or predict and may continue to result in significant disruption of global financial markets, which may have a negative impact on our preclinical studies and clinical trials or reduce our ability to access capital, negatively affecting our liquidity.

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 Lilly Agreement and Novartis Agreement. Under these agreements, we are focused on research and development of *in vivo* gene editing products that utilize or incorporate our ARCUS nucleases. Our likely collaborators for other product research and development arrangements include large and mid-size pharmaceutical and 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, we waived earned, but unpaid milestone payments in connection with the termination of the Servier Agreement. If any of our collaborators terminates its agreement with us, we may be unable to find a suitable 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 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 Lilly and Novartis for certain targets, and during the term of our collaboration agreements 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, or to maintain existing collaborations, 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. For example, in January 2023, we announced that, based on our new prioritized focus, as well as the evolving treatment paradigm for PH1, we have decided to look for a partner in the kidney disease arena for further potential development of PBGENE-PH1 and will no longer develop the program on its own. If we are unable to enter into an appropriate collaboration with respect to PH1 on a timely basis, on acceptable terms, or at all, we may choose to cease related research and development activities. 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 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 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 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 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 continue to 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 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 have been, and may in the future 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 2019, the Patent Trial and Appeal Board (the "PTAB"), of the USPTO initiated two patent interferences involving a family of patents that have been issued to us and a pending patent application filed by a third party. Though the PTAB ultimately found that the third-party patent application did not satisfy written description requirements and rejected the related claims, maintaining the claims in all nine of our patents, any future interference proceedings could result in an adverse outcome, affecting 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 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, 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 foreign 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 foreign 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 EU, 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 and 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 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 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 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 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 (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.

Europe's planned Unified Patent Court may in particular present uncertainties for our ability to protect and enforce our patent rights against competitors in Europe. In 2012, the European Patent Package, or EU Patent Package, regulations were passed with the goal of providing a single pan-European Unitary Patent and a new European Unified Patent Court, or UPC, for litigation involving European patents. Implementation of the EU Patent Package will likely occur in the first half of 2023. Under the UPC, all European patents, including those issued prior to ratification of the European Patent Package, will by default automatically fall under the jurisdiction of the UPC. The UPC will provide our competitors with a new forum to centrally revoke our European patents, and allow for the possibility of a competitor to obtain pan-European injunctions. It will be several years before we will understand the scope of patent rights that will be recognized and the strength of patent remedies that will be provided by the UPC. Under the EU Patent Package as currently proposed, we will have the right to opt our patents out of the UPC over the first seven years of the court's existence, but doing so may preclude us from realizing the benefits of the new unified court.

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 the terms of our Revolving Line 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 the reduced disclosure requirements applicable to emerging growth 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 $1.235 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 may choose to take advantage of some, but not all, of the available exemptions for emerging growth 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 recent past, including severely diminished liquidity and credit availability, declines in consumer confidence, declines in economic growth, increases in unemployment rates, exchange rate impacts 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, 2022, we had cash and cash equivalents of $189.6 million. 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, 2022, 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 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, or healthcare provider 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 33,800 square feet of manufacturing, laboratory and office space used for our MCAT facility 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 1, 2023, there were approximately 26 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 the terms of our Revolving Line, 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. [Reserved].

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, as applicable, on a consolidated basis.

A discussion regarding our financial condition and results of operation, including liquidity and capital resources, for the year ended December 31, 2022 compared to the year ended December 31, 2021 is presented below. A discussion regarding our financial condition and results of operations for the year ended December 31, 2021 compared to the year ended December 31, 2020 is included under "Management's Discussion and Analysis of Financial Condition and Results of Operations" in our Annual Report on 10-K for the year ended December 31, 2021 filed on March 15, 2022.

Overview

We are a clinical stage gene editing company dedicated to improving life by developing *ex vivo* allogeneic chimeric antigen receptor ("CAR") T immunotherapies and *in vivo* therapies for genetic and infectious diseases with the application of our wholly owned proprietary ARCUS genome editing platform. The foundation of ARCUS is a natural homing endonuclease which allows us to replicate precise gene editing as it evolved in nature. ARCUS is designed to be precise in its specificity and versatile in its design for gene knock out as well as complex edits with gene insertion and gene repair. ARCUS is also unique in its relatively small size which potentially allows delivery to a wider range of cells and tissues using viral and non-viral gene delivery methods.

We believe our CAR T cells are the only allogeneic CAR T cells in human clinical trials made with a single gene editing step designed to specifically avoid the potentially deleterious effects of making multiple edits to T cells. We are simultaneously conducting a Phase 1b/2a clinical trial evaluating PBCAR0191, azercabtagene zapreleucel ("azer-cel"), as a potential first-in-class, if approved, and a Phase 1 clinical trial evaluating PBCAR19B as a potential best-in-class, if approved, CD19-targeting CAR T cell therapy in adult patients with relapsed or refractory ("R/R"), B-cell malignancies.

Made from donor-derived T cells modified using our ARCUS genome editing technology, azer-cel recognizes the well characterized tumor cell surface protein CD19, an important and validated target in several B-cell cancers. Azer-cel is designed to avoid graft-versus-host disease, a significant complication associated with donor-derived, cell-based therapies. In June 2022, we provided an interim clinical update and outlined the opportunity for azer-cel for the growing CAR T relapsed patient population with aggressive lymphomas. As of the May 31, 2022 data cutoff, positive efficacy results, including high overall and complete response ("CR") rates and duration of response, and an improved adverse event profile have been observed among evaluable CAR T relapsed subjects. This included six subjects who received azer-cel Dose Level ("DL") 3 of 3×10^6 cells/kg with enhanced lymphodepletion of fludarabine 30 mg/m^2/day × 4 days + cyclophosphamide 1000 mg/m^2/day × 3 days (the "ASH Cohort") and six subjects who received azer-cel DL4b, a flat dose of 500×10^6 cells, with reduced dose lymphodepletion of fludarabine 30 mg/m^2/day × 4 days + cyclophosphamide 750 mg/m^2/day × 3 days since January 2022 (the "New Cohort"). Among 11 subjects evaluable for response, the program update reported efficacy results across both the ASH Cohort and New Cohort, including a 100% (11/11) overall response rate ("ORR") and 73% (8/11) CR rate. Six subjects were in ongoing response (up to 18+ months). In the ASH Cohort, 50% (3/6) of evaluable subjects had a response duration greater than six months. Among subjects treated with DL4b and reduced intensity lymphodepletion in the New Cohort, a 100% CR rate was achieved among evaluable subjects (5/5). One subject was non-evaluable at the Day 28 assessment due to death from suspected fludarabine-associated neurotoxicity on Day 23. The subject had complete resolution of disease according to a CT scan on Day 21.

No Grade 3 or greater cytokine release syndrome was observed in either dosing cohort. One Grade 3 immune effector cell-associated neurotoxicity syndrome was recorded in each cohort that rapidly resolved to Grade 1 within 24 to 48 hours. Two Grade 5 events associated with late occurring encephalopathy suspected to be related to fludarabine-associated neurotoxicity occurred in the New Cohort. There was no evidence of graft versus host disease in either cohort. Grade 3 or greater infections occurred less frequently in the New Cohort with one out of six (17%) subjects compared to four out of six (67%) subjects in the ASH Cohort.

A poster presented at the 64th ASH Annual Meeting in December 2022 evaluated the relationship between healthy cell dose and functional attributes of azer-cel to the efficacy and safety of the product in patients with R/R B-cell lymphoma. This poster showed that post-thaw product composition and healthy CAR T cell dose are predictive for response to treatment with azer-cel. Based on these findings, we have applied optimizations across all allogeneic CAR T platforms with the goal of improving those product attributes and characteristics that drive predictability, reliability, and performance.

In January 2023, we announced we received FDA feedback that we believe signaled alignment with our proposed chemistry, manufacturing and controls ("CMC") plan for azer-cel. In 2023, we intend to progress azer-cel to a decision point for a Phase 2 trial in non-Hodgkin lymphoma ("NHL") subjects who have relapsed following autologous CAR T treatment by completing the Phase 1b cohort to identify a dosing schedule for further study and we plan to seek feedback from the FDA on the azer-cel clinical program once more data become available.

PBCAR19B is a novel immune-evading stealth cell candidate employing a single-gene edit designed to knock-down beta-2 microglobulin in an effort to evade T cell rejection, while also inserting a human leukocyte antigen E transgene to further evade rejection from natural killer cells. As of the June 2022 program update, a flat dose of 270 million cells (DL1) following standard lymphodepletion of fludarabine 30 mg/m^2/day × 3 days + cyclophosphamide 500 mg/m^2/day × 3 days has been administered to three subjects with R/R diffuse large B-cell lymphoma. We are continuing to recruit patients in the PBCAR19B clinical program at DL2 (flat dose of 540 million cells) with the intent to complete the Phase 1 dose escalation in the earlier line NHL setting in 2023.

We plan to provide a CAR T program update once investigators complete enrollment of the current azer-cel cohort of six CAR T relapsed subjects with sufficient follow-up to support a meeting with the FDA to discuss clinical plans. Subjects are being treated with optimized azer-cel product at the planned final dose level (500 million CAR T cells following a lymphodepletion regimen consisting of 3 days of fludarabine and cyclophosphamide). Based on current enrollment, the update is expected to occur in the April/May 2023 time frame, once appropriate follow-up from the current cohort is available. We plan to provide additional long term follow up from the azer-cel cohorts presented at ASH 2021 and ASCO 2022, as well as data from subjects in the current cohort. The CAR T update is also expected to include interim efficacy and safety data from the PBCAR19B Phase 1 trial at Dose Level 2 (540 million CAR T cells following 3 days of fludarabine and cyclophosphamide) with an expectation of durability data to follow this year.

PBCAR269A, an investigational allogeneic CAR T cell candidate targeting B-cell maturation antigen (“BCMA”) for R/R multiple myeloma, when used in combination with nirogacestat, a gamma secretase inhibitor (“GSI”) developed by SpringWorks Therapeutics, Inc., resulted in improved cell expansion, which correlated with increased clinical activity when compared to dose-matched PBCAR269A monotherapy treatment. However, in light of the competitive landscape of BCMA targeted therapies in multiple myeloma, we have made the strategic decision not to continue the PBCAR269A clinical program. All subjects enrolled in the study and evaluated for treatment with PBCAR269A and nirogacestat had acceptable tolerability results.

In vivo gene editing is complex and involves the delivery of ARCUS nucleases directly into a patient’s cells to treat disease at the level of the underlying DNA. We expect the development of *in vivo* therapies for genetic and infectious diseases to be a significant focus of our operations long-term. We believe these applications are particularly well suited to ARCUS because they require extremely low levels of off-target editing and efficient delivery. As a gene editing tool, we believe ARCUS can be differentiated by unique attributes which are designed for precise, specific and versatile gene editing. By nature of its origin from a homing endonuclease, we believe ARCUS has the potential to be particularly applicable to gene insertion and complex edits designed for gene repair aimed at restoring function, as well as more simple gene knock outs. ARCUS is also unique in its relatively small size which potentially allows delivery to a wider range of cells and tissues using viral and non-viral gene delivery methods.

We, along with partners, intend to continue to evaluate the ARCUS platform with regards to safety, on-target editing, gene insertion, complex gene edits, and compatibility with viral and non-viral delivery. Our PBGENE-HBV for the potential treatment of chronic hepatitis B virus (“HBV”) program remains a top priority, and we intend to submit a Clinical Trial Application ("CTA") or Investigational New Drug application ("IND") in 2024. Our gene editing program for chronic HBV applies ARCUS to knock out persistent covalently closed circular DNA and inactivate integrated HBV genomes, potentially achieving durable HBV S-antigen (“HBsAg”) loss and reducing viral persistence. Preclinical data from this program were presented at an oral presentation at the European Society of Gene & Cell Therapy 29th Congress in October 2022 and showed that ARCUS efficiently targeted and degraded HBV cccDNA in HBV-infected primary human hepatocytes and reduced expression of HBV S-antigen (“HBsAg”) by as much as 95%. Similar levels of HBsAg reduction were observed in a newly developed mouse model of HBV infection following administration of ARCUS mRNA using LNP delivery. We plan to present additional data at a scientific conference in 2023.

In June 2022, we announced we entered into an exclusive *in vivo* gene editing research and development collaboration and license agreement (the “Novartis Agreement”) with Novartis Pharma AG (“Novartis”). In connection with this partnership, we are developing a custom ARCUS nuclease that will be designed to insert, *in vivo*, a therapeutic transgene at a “safe harbor” location in the genome as a potential one-time transformative treatment option for diseases including certain hemoglobinopathies such as sickle cell disease and beta thalassemia. Under the terms of the Novartis Agreement, we will develop an ARCUS nuclease and conduct *in vitro* characterization, with Novartis then assuming responsibility for all subsequent research, development, manufacturing and commercialization activities.

We continue our *in vivo* gene editing collaboration with Eli Lilly and Company (“Lilly”) in applying ARCUS nucleases to three initial targets, including Duchenne muscular dystrophy in muscle, a central nervous system directed target and a liver directed target.

In partnership with iECURE, Inc. (“iECURE”), an ARCUS-mediated gene insertion approach is being pursued as a potential treatment for neonatal onset ornithine transcarbamylase ("OTC") deficiency. Non-human primate data presented by researchers from the University of Pennsylvania’s Gene Therapy Program demonstrated sustained gene insertion of a therapeutic OTC transgene one-year post-dosing in newborn and infant non-human primates with high efficiency. A CTA and/or IND filing by iECURE for neonatal onset OTC deficiency is planned for submission in the second half of 2023.

The strategic prioritization exercise for our *in vivo* research pipeline, announced in November 2022, is ongoing to assess diseases with highest unmet need in an increasingly dynamic regulatory and competitive gene editing landscape. We are making trade-offs and further honing our focus on disease areas where we believe ARCUS, more than any other technology, can have the greatest and most profound impact. While we intend to continue to pursue gene knock-out programs opportunistically, the proof of concept data continues to lead toward prioritizing programs involving complex edits and gene insertion (adding a functional copy of a gene) as exemplified by our partnered OTC program. While we remain committed to patients with cardiovascular diseases, we have made the decision to cease pursuit of PBGENE-PCSK9 for familial hypercholesterolemia ("FH") with iECURE as our partner. PCSK9 for FH remains a wholly-owned program, and we are monitoring the regulatory landscape as we consider FH as well as several potential cardiovascular disease indications in our pipeline prioritization exercise.

Work on the PBGENE-PH1 program progressed as planned in 2022. We have clinical candidates ready to proceed to the next stage of IND enabling studies. Based on our new prioritized focus as well as the evolving treatment paradigm for PH1, we have made the choice to look for a partner in the kidney disease arena for further development of PBGENE-PH1 and will no longer develop the program on our own.

In December 2021, we announced our entry into an agreement with a syndicate of investors led by ACCELR8 to separate our then wholly owned subsidiary, Elo Life Systems, Inc. (“Elo”), and create an independent food and agriculture business (“New Elo”). As of December 31, 2022, we held 37% of New Elo's voting shares.

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 through proceeds from upfront and milestone payments from collaboration and licensing agreements, our IPO, private placements of our common stock, convertible preferred stock and convertible debt financings, underwritten and at-the-market offerings of common stock, and borrowings on credit facilities.

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. As of December 31, 2022, we had an accumulated deficit of $428.3 million.

We expect our operating expenses to increase in connection with our ongoing CAR T clinical trials and the expansion of our *in vivo* 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 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.

Collaborations

Novartis Pharma AG

On June 14, 2022, we entered into the Novartis Agreement, which became effective on June 15, 2022 (the "Novartis Effective Date"), to collaborate to discover and develop *in vivo* gene editing products incorporating our custom ARCUS nucleases for the purpose of seeking to research and develop potential treatments for certain diseases (as defined in the Novartis Agreement, the "Licensed Products"). Any initial Licensed Products will be developed for the potential treatment of certain hemoglobinopathies, including sickle cell disease and beta thalassemia.

Pursuant to the terms of the Novartis Agreement, we will develop an ARCUS nuclease and conduct *in vitro* characterization for the Licensed Products, with Novartis then assuming responsibility for all subsequent development, manufacturing and commercialization activities. Novartis will receive an exclusive license for, and be required to use commercially reasonable efforts to conduct all subsequent research, development, manufacture and commercialization activities with respect to the Licensed Products. We will initially develop a single, custom ARCUS nuclease for a defined "safe harbor" target site for insertion of specified therapeutic payloads in the patient's genome (the "Initial Nuclease") for Novartis to further develop as a potential *in vivo* treatment option for certain hemoglobinopathies, including sickle cell disease and beta thalassemia. Pursuant to the terms of the Novartis Agreement, Novartis may elect, subject to payment of a fee to us, to replace Licensed Products based on the Initial Nuclease with Licensed Products based on a second custom ARCUS nuclease we design for gene editing of a specified human gene target associated with hemoglobinopathies (the "Replacement Nuclease"). Additionally, Novartis has the option, upon payment of a fee to us for each exercise of the option, to include Licensed Products utilizing the Initial Nuclease for insertion of up to three additional specified therapeutic payloads at the "safe harbor" target site, each intended to treat a particular genetic disease. The exercise period for such option ends on the earlier of (a) the fourth anniversary of the Novartis Effective Date and (b) the replacement of the Initial Nuclease with the Replacement Nuclease as described above.

In July 2022, we received a $50.0 million upfront cash payment under the Novartis Agreement. Additionally, on the Novartis Effective Date, Novartis made an equity investment in our common stock pursuant to a stock purchase agreement (the "Novartis Stock Purchase Agreement") pursuant to which, on the Novartis Effective Date, we issued and sold to Novartis 12,407,440 shares of our common stock (the "Novartis Shares") in a private placement transaction for an aggregate purchase price of $25.0 million, or approximately $2.01 per share. The price per share of our common stock under the Novartis Stock Purchase Agreement represented a 20% premium over the volume-weighted-average-price of our common stock over the 10 trading days preceding the execution date of the Novartis Stock Purchase Agreement.

Pursuant to the Novartis Stock Purchase Agreement, subject to certain exceptions, Novartis may not sell the Novartis Shares without our approval for a period of two years following the Novartis Effective Date. In addition, for a period of two years following the Novartis Effective Date, Novartis and its affiliates may not (a) effect or otherwise participate in, directly or indirectly, any acquisition of any of our securities or material assets, any tender offer or exchange offer, merger or other business combination or change of control involving us, any recapitalization, restructuring, liquidation, dissolution or other extraordinary transaction with respect to us, or any solicitation of proxies or consents to vote any of our securities or (b) act with any other person, or publicly disclose any intention, to do any of the foregoing. The Novartis Stock Purchase Agreement also contains customary representations, warranties, and covenants of both parties.

On the Novartis Effective Date, we and Novartis also entered into a registration rights agreement (the "Registration Rights Agreement") pursuant to which we have agreed, within the time periods specified in the Registration Rights Agreement, to register the resale of the Novartis Shares on a registration statement to be filed with the SEC. The Registration Rights Agreement contains customary indemnification provisions, and all registration rights terminate in their entirety effective on the first date on which there cease to be any Registrable Securities (as defined in the Registration Rights Agreement) outstanding.

We will also be eligible to receive milestone payments of up to an aggregate of approximately $1.4 billion as well as 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 to low-double digit percentages on net sales of Licensed Products, subject to customary potential reductions. Novartis'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 the first commercial sale of the Licensed Product.

Unless earlier terminated, the Novartis 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. Novartis has the right to terminate the Novartis Agreement without cause by providing advance notice to us. Either party may terminate the Novartis Agreement for material breach by the other party and a failure to cure such breach within the time period specified in the Novartis Agreement. We may also terminate the Novartis Agreement in the event that Novartis brings a challenge to our patents.

During the year ended December 31, 2022 we recognized revenue under the Novartis Agreement of $9.5 million. Deferred revenue related to the Novartis Agreement amounted to $54.2 million as of December 31, 2022, of which $27.9 million was included in current liabilities within the consolidated balance sheets.

Eli Lilly and Company

In January 2021, we closed a development and license agreement, subsequently amended by the First Amendment to the Development and License Agreement dated August 9, 2021 (as amended, the "Lilly Agreement") with Lilly to utilize ARCUS for the research and development of potential *in vivo* therapies for genetic disorders. Lilly has initially nominated Duchenne muscular dystrophy ("DMD"), a liver-directed target and a central nervous system directed target, and has the right to nominate up to three additional gene targets for genetic disorders over the initial nomination period of four years (the "Nomination Period"). Lilly may extend the Nomination Period for an additional two years from the date on which the Nomination Period ends, upon Lilly's election and payment of an extension fee. Under the terms of the Lilly Agreement, Lilly received 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 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 (the "Lilly Share Purchase Agreement"). We 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, 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 or CTA 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 Lilly 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 Lilly Agreement.

Unless earlier terminated, the Lilly 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 Lilly Agreement for convenience by providing advance notice to us. Either party may terminate the Lilly 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.

During the years ended December 31, 2022 and 2021, we recognized revenue under the Lilly Agreement of approximately $15.6 million and $21.0 million, respectively. Deferred revenue related to the Lilly Agreement amounted to $74.8 million and $88.3 million as of December 31, 2022 and 2021, of which $18.3 million and $21.2 million, respectively, was included in current liabilities within the consolidated balance sheets.

iECURE

In August 2021, we entered into the iECURE Agreement. We have made the decision to cease pursuit of PBGENE-PCSK9 for FH with iECURE as our partner. Pursuant to the iECURE Agreement, we retain the rights to PBGENE-PCSK9, including all products developed for genetic indications with increased risk of severe cardiovascular events such as FH. In conjunction with the iECURE Agreement, we also granted iECURE a license to use our PCSK9-directed ARCUS nuclease to insert genes into the PCSK9 locus to develop treatments for four other pre-specified rare genetic diseases, including OTC deficiency, Citrullinemia Type 1 ("CTLN1"), Phenylketonuria ("PKU"), and another program focused on liver disease. Simultaneously with the entry into the iECURE Agreement, we and iECURE entered into an Equity Issuance Agreement (the "iECURE Equity Issuance Agreement"), pursuant to which iECURE issued us common stock in iECURE as additional consideration for the PCSK9 license. Additionally, the Company is eligible to receive milestone and mid-single digit to low double digit royalty payments on sales of iECURE products developed with ARCUS.

The fair value of the iECURE equity at inception of the iECURE agreements was assessed to be $0.5 million and was initially recorded to the investment in equity securities line item of the consolidated balance sheets. As further discussed in Note 4, *Fair Value Measurements,* to our Financial Statements, on issuance, Management elected to account for the iECURE equity at fair value under accounting standards codification ("ASC") 825. Accordingly, we adjust the carrying value of the iECURE equity to fair value each reporting period with any changes in fair value recorded to other income (expense). In the year ended December 31, 2022 we recorded a $0.5 million decrease in the carrying value of our iECURE equity to adjust to fair value as a result of dilution from iECURE's Series A-1 equity raise in such period. The fair value of the costs to be incurred by iECURE to progress our PBGENE-PCSK9 candidate through Phase 1 clinical trial (the "PCSK9 Prepaid") was assessed to be $17.4 million and was recorded to the prepaid expenses and other assets line items of the consolidated balance sheets. The PCSK9 Prepaid was amortized to research and development expense on a pro-rata basis as iECURE incurred costs to progress the PBGENE-PCSK9 candidate through the Phase 1 clinical trial.

As further discussed in Note 11, *Impairment Charges,* to our Financial Statements, the remaining unamortized PCSK9 Prepaid was fully impaired during the year ended December 31, 2022, as we have made the decision to cease pursuit of PBGENE-PCSK9 for FH with iECURE as our partner. Accordingly, there was no PCSK9 Prepaid balance as of December 31, 2022. As of December 31, 2021 the remaining balance of the PCSK9 Prepaid was $13.0 million, which was included in the prepaid expenses and other assets line items of the consolidated balance sheets in the amounts of $10.4 million and $2.6 million, respectively.

During the year ended December 31, 2022, we recognized no revenue under the iECURE agreements. During the year ended December 31, 2021, we recognized $17.9 million of revenue under the iECURE agreements. During the years ended December 31, 2022 and 2021, we recognized $2.1 million and $4.4 million of research and development expense related to amortization of the PCSK9 Prepaid.

Servier

In February 2016, we entered into the Servier Agreement with Servier, pursuant to which we agreed to develop allogeneic CAR T cell therapies for five unique antigen targets. One target was selected at the Servier 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. Upon selection of an antigen target under the Servier Agreement, we 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.

On April 9, 2021, we entered into the Program Purchase Agreement with Servier, pursuant to which we reacquired all of our global development and commercialization rights previously granted to Servier pursuant to the Servier Agreement, and mutually terminated the Servier Agreement.

Pursuant to the Servier Agreement, we had developed certain allogeneic CAR T candidates, including azer-cel and the stealth cell PBCAR19B, each targeting CD19, as well as four additional product targets under the Servier Agreement. Pursuant to the terms of the Program Purchase Agreement, we regained full global rights to research, develop, manufacture and commercialize products resulting from such programs, with sole control over all activities. Additionally, per the terms of the Program Purchase Agreement we do not have an obligation to continue development of the Servier Targets. With respect to products directed to CD19, Servier has certain rights of negotiation, which may be exercised during a specified time period if we elect to initiate a process or entertain third party offers for partnering such products.

Pursuant to the terms of the Program Purchase Agreement, we made a payment of $1.25 million in cash to Servier and agreed to waive earned milestones totaling $18.75 million that would have been otherwise payable to us.

The Program Purchase Agreement also requires us to make certain payments to Servier based on the achievement of regulatory and commercial milestones for each product, and a low- to mid-single-digit percentage royalty (subject to certain reductions) based on net sales of approved products, if any, resulting from our continued development and commercialization of the programs, for a period not to exceed ten years after first commercial sale of the applicable product in the United States or certain countries in Europe. If we enter into specified product partnering transactions, the Program Purchase Agreement requires us to pay to Servier a portion of certain consideration received pursuant to such product partnering transactions in lieu of the foregoing milestones (with the exception of a one-time clinical phase development milestone) and royalties. For additional discussion of accounting for payment obligations arising from the Program Purchase Agreement, refer to Note 6, *Commitments and Contingencies,* to our Financial Statements.

We recognized no revenue under the agreement with Servier during the year ended December 31, 2022. During the year ended December 31, 2021, we recognized revenue under the agreement with Servier of approximately $72.9 million. We did not have deferred revenue related to the agreement with Servier as of December 31, 2022 or December 31, 2021.

Tiziana

In September 2021, we entered into an exclusive license agreement to evaluate Tiziana's foralumab, a fully human anti-CD3 monoclonal antibody, as a lymphodepleting agent in conjunction with our allogeneic CAR T cells for the potential treatment of cancers. We plan to assess foralumab use in combination with an allogeneic CAR T.

SpringWorks Therapeutics

In September 2020, we entered into a Clinical Trial Collaboration Agreement with SpringWorks Therapeutics, Inc. Pursuant to such agreement, PBCAR269A was evaluated in combination with nirogacestat, SpringWorks' investigational gamma secretase inhibitor, in patients with R/R multiple myeloma. Under the terms of the agreement, we were responsible for all costs associated with the conduct of the clinical trial including providing PBCAR269A for use in the trial, and SpringWorks was responsible for providing nirogacestat at its sole cost and expense. The combination therapy and increased dose of PBCAR269A resulted in improved cell expansion, which correlated with increased clinical activity when compared to dose-matched PBCAR269A monotherapy treatment. However, in light of the competitive landscape of BCMA targeted therapies in multiple myeloma, we have made the strategic decision not to continue the PBCAR269A clinical program.

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. In April 2020, both parties agreed to coordinate a wind-down of all activities in their entirety under the agreement, effective as of June 2020, however, in August 2020 and subsequently in January 2021, both parties agreed to extend certain portions of the agreement through 2022. We will not be required to make termination payments to Penn.

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 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 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 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.

Research and development activities are central to our business model. We expect that our research and development expenses will increase over the long term and will comprise a larger percentage of our total expenses as we continue our clinical trials for our *ex vivo* allogeneic CAR T immunotherapies and development of our *in vivo* therapies for genetic and infectious diseases.

We cannot determine with certainty the duration and costs of ongoing and future clinical trials of our azer-cel and PBCAR19B 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 azer-cel and PBCAR19B 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 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 the COVID-19 pandemic and variants thereof or any similar pandemic;
- 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, legal 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 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 to meet our growing infrastructure needs as we progress our clinical trials and move toward commercialization.

Impairment Charges

Impairment charges represents our impairment of intangible assets and long-term prepaid assets. 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. An impairment charge is recognized for the amount by which the carrying amount exceeds the fair value of the asset.

Loss on Disposal of Assets

Loss on disposal of assets represents the remaining net book value of disposed assets at the time of their disposal.

(Loss) Gain from Changes in Fair Value

(Loss) gain from changes in fair value represents the assessed change in fair value of assets and liabilities carried at fair value between reporting periods.

Gain on Deconsolidation of Subsidiary

The gain on deconsolidation of subsidiary was determined based on the difference between the book value of the net assets that we contributed to New Elo as part of the Elo Transaction as well as the fair value of the promissory note we received from New Elo ("Note Receivable") and the fair value of our ownership in New Elo as of December 17, 2021.

(Loss) Income from Equity Method Investments

(Loss) income from equity method investments represents changes in the carrying value of our investment in New Elo.

Interest Expense

Interest expense consists of interest payments incurred and discount amortization on debt outstanding.

Interest Income

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

Income Taxes

Since our inception in 2006, we have generated cumulative federal and state NOL and 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, 2022, we had federal and state NOL carryforwards of $159.5 million and $119.1 million, respectively, which may be available to offset future taxable income. The U.S. federal NOLs carryforward indefinitely. The state NOL carryforwards begin to expire in 2027. As of December 31, 2022, we also had federal and state R&D tax credit carryforwards of $13.2 million and an amount less than $0.1 million, which begin to expire in 2027 and 2030, respectively. As of December 31, 2022 and December 31, 2021, we had federal Orphan Drug credits of $11.6 million and $9.5 million, respectively, which begin to expire in 2038. As of December 31, 2022, we also have federal contribution carryforwards of $0.2 million, which began to expire in 2022. We have recorded a full valuation allowance against our net deferred tax assets at each balance sheet date.

Results of Operations

Comparison of the Years Ended December 31, 2022 and December 31, 2021

The following table summarizes our results of operations for the years ended December 31, 2022 and December 31, 2021, together with the changes in those items in dollars:

(in thousands)	Years ended December 31, 2022	2021	Change
Revenue	$ 25,098	$ 115,529	$ (90,431)
Operating expenses:			
Research and development	83,939	115,238	(31,299)
General and administrative	41,525	39,667	1,858
Total operating expenses	125,464	154,905	(29,441)
Loss from operations	(100,366)	(39,376)	(60,990)
Other (expense) income, net:			
Impairment charges	(11,438)	—	(11,438)
Loss on disposal of assets	(106)	(26)	(80)
(Loss) gain from changes in fair value	(510)	2,555	(3,065)
Gain on deconsolidation of subsidiary	—	5,985	(5,985)
(Loss) income from equity method investment	(1,579)	184	(1,763)
Interest expense	(1,111)	(132)	(979)
Interest income	3,473	208	3,265
Total other (expense) income, net	(11,271)	8,774	(20,045)
Net loss	$ (111,637)	$ (30,602)	$ (81,035)

Revenue

Revenue for the year ended December 31, 2022 was $25.1 million, compared to $115.5 million for the year ended December 31, 2021. The decrease of $90.4 million in revenue during the year ended December 31, 2022 was primarily the result of $72.9 million in revenue recognized under the Servier Agreement in 2021 that did not occur in 2022, following satisfaction of the performance obligation upon the execution of the Program Purchase Agreement in April 2021, a $17.9 million decrease in revenue recognized under the iECURE Agreement as the performance obligation was deemed fully satisfied in August 2021 upon the grant of the PCSK9 license to iECURE, a $5.4 million decrease in revenue recognized under the Lilly Agreement as a result of an increase in total estimated effort required to satisfy the performance obligation, and a $3.7 million decrease in revenue recognized from agriculture partnering collaborations given the collaboration transferred to New Elo upon separation in December 2021. These decreases in revenue were partially offset by a $9.5 million increase in revenue recognized under the Novartis Agreement, as work thereunder began during 2022.

Research and Development Expenses

(in thousands)	Years ended December 31, 2022	2021	Change
Direct research and development expenses by product candidate:			
Azer-cel external development costs	$ 5,502	$ 8,486	$ (2,984)
PBCAR19B external development costs	2,111	2,948	(837)
BCMA external development costs	1,600	3,337	(1,737)
CD20 external development costs	372	3,666	(3,294)
Platform development and early-stage research expenses:			
Employee-related costs (other than share based compensation)	29,889	32,519	(2,630)
Share based compensation	7,973	9,101	(1,128)
Program Purchase Agreement costs and contract liability	—	11,250	(11,250)
Amortization of PCSK9 Prepaid	2,091	4,421	(2,330)
Laboratory supplies and services	13,156	14,529	(1,373)
Sublicensing royalty payable to Duke	1,500	1,111	389
Outsourced research and development	5,272	2,336	2,936
CMOs and research organizations	864	5,347	(4,483)
Laboratory equipment and maintenance	1,320	2,065	(745)
Facility-related costs	2,881	3,562	(681)
Depreciation and amortization	6,594	7,574	(980)
Licensing fees	2,729	2,585	144
Other research and development costs	85	401	(316)
Total research and development expenses	$ 83,939	$ 115,238	$ (31,299)

Research and development expenses for the year ended December 31, 2022 were $83.9 million, compared to $115.2 million for the year ended December 31, 2021. The decrease of $31.3 million was primarily due to a decrease of $11.3 million in expense related to the Program Purchase Agreement, which was comprised of a $10.0 million financial contract liability that was accrued as it was deemed probable to occur and a $1.3 million cash payment to Servier that was recorded to expense in the year ended December 31, 2021.

Additionally, there was a decrease of $8.9 million in direct research and development expenses related to our allogeneic CAR T product candidates, including $1.7 million and $3.3 million decreases in BCMA and CD20 external development costs, respectively, as the result of our decision not to continue clinical development of PBCAR269A and PBCAR20A, a $3.0 million decrease in azer-cel external development expense driven by lower CRO expense as a result of lower patient activity as IRBs reviewed our updated lymphodepletion regimen and operational efficiencies, and a $0.8 million decrease in PBCAR19B external development costs driven by a milestone fee paid in the year ended December 31, 2021 related to patient dosing.

Further contributing to the decrease in research and development expenses during the year ended December 31, 2022 were decreases of $2.6 million, $1.1 million, $1.4 million, $1.0 million, and $0.6 million in employee-related costs, share based compensation, laboratory supplies and services, depreciation and amortization expense, and facility-related costs, respectively, driven by the separation of Elo in 2021. Additionally, unallocated CMO and research organization expense related to our preclinical studies decreased $4.5 million which was primarily driven by the completion of CMO manufacturing programs, and expense related to the amortization of the iECURE PCSK9 Prepaid decreased by $2.3 million as a result of the decision to cease pursuit of PBGENE-PCSK9 for FH with iECURE as our partner. These decreases were partially offset by a $2.9 million increase in outsourced research and

development costs in the year ended December 31, 2022 as compared to the year ended December 31, 2021, which were primarily related to preclinical studies for our *in vivo* gene editing programs and consulting fees.

General and Administrative Expenses

General and administrative expenses were $41.5 million for the year ended December 31, 2022 compared to $39.7 million for the year ended December 31, 2021. The increase of $1.8 million was primarily due to an increase of $3.8 million in share-based compensation expense. This increase was partially offset by a $0.7 million decrease in insurance expense primarily driven by a reduction in director and officer insurance premiums, a $0.8 million decrease in legal expense, and a $0.5 million decrease in information technology expense related to software subscriptions.

Impairment Charges

Impairment charges were $11.4 million during the year ended December 31, 2022 which includes the $10.8 million impairment of the iECURE PCSK9 Prepaid as we have made the decision to cease pursuit of PBGENE-PCSK9 for FH with iECURE as our partner. The impairment charge represented the remaining unamortized balance of the PCSK9 Prepaid. Additionally included in impairments of long lived assets during the year ended December 31, 2022 were intangible asset impairment charges of $0.6 million related to licensed technology rights that are no longer in use. There were no impairment charges in the year ended December 31, 2021.

Loss on Disposal of Assets

Loss on disposal of assets was $0.1 million during the year ended December 31, 2022 compared to less than $0.1 for the year ended December 31, 2021 which represented the remaining net book value of property, equipment and software at the time of their disposal.

(Loss) Gain from Changes in Fair Value

The loss from changes in fair value was $0.5 million for the year ended December 31, 2022 which primarily represents the change in fair value of the iECURE equity investment as a result of dilution from iECURE's Series A-1 equity raise during the year ended December 31, 2022. The change in fair value of investment was $2.6 million for the year ended December 31, 2021 which was attributed to an increase in the assessed fair value of our equity investment in iECURE from issuance in August 2021 to December 31, 2021.

Gain on Deconsolidation of Subsidiary

There was no gain on deconsolidation of subsidiary in the year ended December 31, 2022. The gain on deconsolidation of subsidiary was $6.0 million for the year ended December 31, 2021 and represents the difference between the book value of the net assets that we contributed to New Elo as part of the Elo Transaction and the sum of the fair value of the Note Receivable and the fair value of our Ownership in New Elo as of December 17, 2021.

(Loss) Income from Equity Method Investments

Loss from equity method investments was $1.6 million during the year ended December 31, 2022 and represented our proportionate share of New Elo’s net loss for such period, partially offset by a gain recorded from an increase in our proportionate share of New Elo's net assets resulting from an equity issuance by New Elo. For the year ended December 31, 2021, we had income from equity method investments of $0.2 million which represented our proportionate share of New Elo’s net income from December 18, 2021 through December 31, 2021.

Interest Expense

Interest expense was $1.1 million for the year ended December 31, 2022 compared to $0.1 million during the year ended December 31, 2021. The $1.0 million increase in interest expense was the result of an increase in debt outstanding coupled with higher stated and effective interest rates on our debt.

Interest Income

Interest income was $3.5 million during the year ended December 31, 2022 compared to $0.2 million during the year ended December 31, 2021. The $3.3 million increase in interest income during the year ended December 31, 2022 was driven by a larger cash balance and higher interest rates as compared to the year ended December 31, 2021 coupled with interest income on the $10.0 million Note Receivable due from New Elo that was issued in December 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 over the long term, 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.

As of December 31, 2022, we had cash and cash equivalents of $189.6 million and available borrowings of $7.5 million. Our sources of funding have historically included proceeds from third parties through a combination of financings including our IPO, preferred stock and convertible note financings, underwritten offerings of our common stock, at-the-market offerings of our common stock as part of our shelf registration statement, upfront and milestone payments from customers, borrowings under bank facilities 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, 2022, we had sold 3,187,508 shares of our common stock in at-the-market offerings as part of our shelf registration statement, resulting in net proceeds of $28.1 million, after deducting agent commissions and issuance costs. Additionally, in June 2022, pursuant to our Form S-3, we issued and sold 35,971,224 shares of our common stock at an offering price of $1.39 per share, less underwriting discounts and commissions, and received approximately $46.7 million in net proceeds.

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 global macroeconomic conditions and ongoing uncertainty related to the COVID-19 pandemic and variants thereof. 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 variants thereof 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 the COVID-19 Pandemic" above and "*Risk Factors— COVID-19 has impacted, and may continue to impact, 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 and its variants 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 through proceeds from upfront and milestone payments from collaboration and licensing agreements, our IPO, private placements of our common stock, convertible preferred stock and convertible debt financings, underwritten and at-the-market offerings of common stock, and borrowings on credit facilities.

Cash Flows

Our cash and cash equivalents totaled $189.6 million as of December 31, 2022, compared to $143.7 million as of December 31, 2021.

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

	For the Years Ended December 31,	
(in thousands)	**2022**	**2021**
Net cash used in operating activities	$ (45,753)	$ (10,853)
Net cash used in investing activities	(3,319)	(5,803)
Net cash provided by financing activities	94,985	70,521
Increase in cash and cash equivalents	$ 45,913	$ 53,865

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, 2022 and December 31, 2021 resulted from our net loss adjusted for non-cash items and changes in working capital.

Cash used in operating activities during the year ended December 31, 2022 was $45.8 million, compared to $10.9 million during the year ended December 31, 2021. The increase in cash used in operating activities in the year ended December 31, 2022 was primarily driven by the $100.0 million upfront payment received from Lilly in January 2021, partially offset by the $50.0 million upfront payment received from Novartis in July 2022.

Cash Used in Investing Activities

Cash used in investing activities primarily relates to cash expenditures to acquire leasehold additions, equipment, software, and intangible assets. Net cash used in investing activities during the year ended December 31, 2022 was $3.3 million, compared to $5.8 million in the year ended December 31, 2021. The $2.5 million decrease in cash used in investing activities during the year ended December 31, 2022 was driven by a decrease in cash expenditures for purchases of laboratory equipment for our MCAT facility as well as a $0.8 million cash expenditure for the license to evaluate Tiziana's foralumab as a lymphodepletion agent in conjunction with our allogeneic CAR T therapeutics, which was capitalized as an intangible asset during the year ended December 31, 2021.

Cash Provided by Financing Activities

Net cash provided by financing activities during the year ended December 31, 2022 was $95.0 million, compared to $70.5 million during the year ended December 31, 2021. The increase in cash provided by financing activities during the year ended December 31, 2022 was primarily due to a $23.9 million increase in net proceeds from offerings of common stock in the year ended December 31, 2022 as compared to the year ended December 31, 2021. Additionally contributing to the increase in cash provided by financing activities in the year ended December 31, 2022 was an increase of $17.3 million in net proceeds from debt borrowings. These increases were partially offset by a $10.0 million decrease in proceeds from the issuance of common stock to collaboration partners, and a $6.4 million decrease in proceeds from stock option exercises in the year ended December 31, 2022 as compared to the year ended December 31, 2021.

Debt Obligations

Revolving Line

We may request advances on our loan and security agreement (as amended from time to time, the "Revolving Line") with Pacific Western Bank ("PWB") up to an aggregate principal of $30.0 million. In July 2022, the Revolving Line maturity date was extended to June 23, 2024 upon receipt of $100.0 million in aggregate new gross proceeds (as defined in the Revolving Line). All outstanding principal amounts are due upon maturity. We 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 interest rate on Revolving Line borrowings is a variable annual rate equal to the greater of (a) 0.75% above the Prime Rate (as defined in the Revolving Line), or (b) 4.25%. As of December 31, 2022, the outstanding principal balance on the Revolving Line was $22.5 million, the stated interest rate was 8.25% and the effective interest rate was 9.27%.

Funding Requirements

As a clinical stage company, we will continue to have funding requirements in connection with the continuation of our current clinical trials and planned initiation of additional clinical trials, potential IND, CTA and BLA filings, and expected growth in our *ex vivo* and *in vivo* portfolios.

We believe that, as of the date of this Annual Report on Form 10-K, existing cash and cash equivalents, continued operational discipline, and available credit will allow us to fund operating expense and capital expenditure requirements through the first quarter of 2025. 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 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 azer-cel and PBCAR19B programs as we progress clinical trials, including CRO costs;
- the progress, costs and results of our additional research and preclinical development programs including our *in vivo* and *ex vivo* pipeline and our planned IND or CTA submissions and potential BLA filings;

- 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 azer-cel and PBCAR19B 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. See "*Risk Factors – 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."* in Part I, Item 1A. of this Annual Report on Form 10-K for a further discussion of our ability to generate and obtain adequate amounts of funding in connection with our continuing operations.

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 and Commitments

The following is a summary of our contractual obligations and commitments as of December 31, 2022:

	Payments Due by Period				
(in thousands)	Total	Less Than 1 Year	1-3 Years	3-5 Years	More than 5 Years
Lease Obligations[1]	$ 7,820	$ 2,822	$ 3,165	$ 1,833	$ —
Revolving Line of Credit[2]	25,290	1,882	23,408	—	—
Total	$ 33,110	$ 4,704	$ 26,573	$ 1,833	$ —

(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, 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, 2022 (see Note 6, *Commitments and Contingencies*, to the Financial Statements.

(2) Represents principal and estimated interest payments on our $22.5 million in outstanding Revolving Line borrowings as of December 31, 2022. Under the Revolving Line we may request advances on a revolving line of credit of up to an aggregate principal of $30.0 million. In May 2022, the Company and PWB executed the Seventh Amendment to the Revolving Line (the "Revolving Line Amendment"). Upon the execution of the Revolving Line Amendment, the interest rate on credit advances was

modified to the greater of (a) 0.75% above the Prime rate (as defined in the Revolving Line) and (b) 4.25%. In July 2022, the maturity date of the Revolving Line was extended to June 23, 2024 upon the Company's receipt of $100.0 million in aggregate new gross proceeds (as defined in the Revolving Line Amendment). All outstanding principal amounts under the Revolving Line are due on the maturity date. As of December 31, 2022, the stated interest rate on the Revolving Line was 8.25% and the effective interest rate was 9.27%.

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 Financial Statements, which have been prepared in accordance with accounting principles generally accepted in the United States ("GAAP"). The preparation of our 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 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 Financial Statements, we believe that the following accounting policies are those most critical to the judgments and estimates used in the preparation of our 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.

ASC 606, *Revenue from Contracts with Customers,* 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 current assets 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.

The Company analyzes its collaboration arrangements to assess whether they are within the scope of ASC 808, *Collaborative Arrangements*, 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.

Revenue related to performance obligations satisfied over time could be materially impacted as a result of changes in the estimated research effort to satisfy performance obligations or changes in the transaction price related to variable consideration. For example, in in the year ended December 31, 2022, we recorded cumulative catch up adjustments that decreased revenue recognition by $5.9

million as a result of changes in total estimated effort required to satisfy performance obligations. If we were to increase total estimated effort required to satisfy the performance obligations by 10%, it would result in cumulative catch up adjustments that decrease revenue recognition by $4.2 million in the current year and those amounts would be recognized in the future as the incremental effort is provided. Alternatively, if we were to decrease total estimated effort required to satisfy the performance obligations by 10%, it would result in cumulative catch up adjustments that increase revenue recognition by $5.1 million in the current year.

Accrued Research and Development Expenses

As part of the process of preparing our consolidated financial statements, we are required to make certain estimates and judgements in 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. Actual costs incurred could differ materially from estimates. 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.

The fair value of each stock option grant is estimated 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 the stock options, the risk-free interest rate for a period that approximates the expected term of the stock options and the our expected dividend yield. Expected volatility is estimated based on the historical volatility of our and other comparable publicly traded peer companies. The expected term of the options has been determined utilizing a weighted average 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 does not expect to pay any cash dividends in the foreseeable future.

The fair value of each restricted stock unit is determined based on the closing market price of our common stock on the date of grant.

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, *Description of Business and Summary of Significant Accounting Policies*, to our Financial Statements.

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 $1.235 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 $189.6 million, or 80% of our total assets, on December 31, 2022 and $143.7 million, or 68% of our total assets, on December 31, 2021. Interest income earned on these assets was $3.5 million and $0.2 million for the years ended December 31, 2022 and December 31, 2021, 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 material impact on our financial statements. A hypothetical 10% change in existing interest rates would not have had a material impact on the value of our cash and cash equivalents as of December 31, 2022.

We are also exposed to foreign exchange rate risk with respect to 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 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 Chief Financial Officer concluded that our disclosure controls and procedures were effective at the reasonable assurance level as of December 31, 2022.

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, 2022, 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, 2022 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information.

None.

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections.

None.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

INFORMATION ABOUT OUR DIRECTORS & EXECUTIVE OFFICERS

The following information with respect to our board of directors and executive officers is presented as of March 9, 2023:

Name	Age	Position at Precision BioSciences, Inc.	Principal Employment
Executive Officers			
Michael Amoroso	45	President, Chief Executive Officer and Director	Same
John Alexander Kelly	56	Chief Financial Officer	Same
Alan List, M.D.	68	Chief Medical Officer	Same
Dario Scimeca	48	General Counsel and Secretary	Same
Jeff Smith, Ph.D.	50	Chief Research Officer	Same
Non-Employee Directors			
Kevin Buehler	65	Chair of the Board and Director	Former Division Head of Alcon Laboratories, Inc. a division of Novartis AG
Melinda Brown	66	Director	Chief Financial Officer of The Draft Network
Stanley Frankel, M.D.	64	Director	Former Chief Medical Officer of Cytovia Therapeutics, Inc.
Geno Germano	62	Director	President, Chief Executive Officer and Director of Elucida Oncology, Inc.
Shari Lisa Piré, J.D.	58	Director	Chief Legal & Sustainability Officer at Plume Design, Inc.
Sam Wadsworth, Ph.D.	74	Director	Senior Scientific Advisor of Ultragenyx Pharmaceuticals, Inc.

The information required by this item will be included in our definitive proxy statement ("2023 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 2023 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 2023 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 2023 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 2023 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 and Financial Statement Schedules.

(a)(1) Financial Statements

The following documents are included on pages F-1 through F-27 attached hereto and are filed as part of this Annual Report on Form 10-K.

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

(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, furnished or incorporated by reference 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-K	00138841	4.5	3/15/2022	
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††	Program Purchase Agreement by and among Les Laboratoires Servier, Institut de Recherches Internationales Servier, and Precision BioSciences, Inc., dated April 9, 2021.	10-Q	001-38841	10.1	5/13/2021	
10.6††	Development and License Agreement between Eli Lilly and Company and Precision BioSciences, Inc., dated November 19, 2020.	10-K	001-38841	10.5	3/18/2021	
10.7††	First Amendment to Development and License Agreement between Precision BioSciences, Inc. and Eli Lilly and Company, dated August 9, 2021.	10-Q	001-38841	10.2	11/10/2021	
10.8	Stock Purchase Agreement between Eli Lilly and Company and Precision BioSciences, Inc., dated November 19, 2020.	10-K	001-38841	10.6	3/18/2021	
10.9††	Collaboration and License Agreement, dated June 14, 2022, by and between Precision BioSciences, Inc. and Novartis Pharma AG.	8-K	001-38841	10.1	6/21/2022	
10.10††	Stock Purchase Agreement, dated June 14, 2022, by and between Precision BioSciences, Inc. and Novartis Pharma AG.	8-K	001-38841	10.2	6/21/2022	
10.11	Registration Rights Agreement, dated June 15, 2022, by and between Precision BioSciences, Inc. and Novartis Pharma AG.	8-K	001-38841	10.3	6/21/2022	

Exhibit Number	Description	Form	File No.	Exhibit	Filing Date	Filed Herewith
10.12†	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	
10.13†	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	
10.14	Lease Agreement between Precision BioSciences, Inc. and Venable Tenant, LLC, dated April 5, 2010, as amended.	10-K	001-38841	10.9	3/18/2021	
10.15	Lease Agreement between Precision BioSciences, Inc. and Durham TW Alexander, LLC, dated October 2, 2018, as amended.	10-K	001-38841	10.12	3/15/2022	*
10.16#	2006 Stock Incentive Plan, as amended, and form of award agreements thereunder.	S-1	333-230034	10.8	3/1/2019	
10.17#	2015 Stock Incentive Plan, as amended, and form of award agreements thereunder.	S-1	333-230034	10.9	3/1/2019	
10.18#	2019 Incentive Award Plan, and forms of award agreements thereunder.	10-K	001-38841	10.14	3/18/2021	
10.19#	2019 Employee Stock Purchase Plan.	S-1/A	333-230034	10.11	3/18/2019	
10.20#	2021 Employment Inducement Incentive Award Plan and form of award agreements thereunder.	S-8	333-259369	99.3	9/7/2021	
10.21#	Amendment to the Precision BioSciences, Inc. 2021 Employment Inducement Incentive Award Plan.	S-8	333-267079	99.4	8/26/2022	
10.22#	Amended and Restated Executive Employment Agreement between Precision BioSciences, Inc. and Alex Kelly, dated November 7,2022.					*
10.23#	Amended and Restated Executive Employment Agreement between Precision BioSciences, Inc. and Dr. Alan List, dated November 7,2022.					*
10.24#	Amended and Restated Executive Employment Agreement between Precision BioSciences, Inc. and Dario Scimeca, dated November 7,2022.					*
10.25#	Amendment to Executive Employment Agreement between Precision BioSciences, Inc. and Dr. Derek Jantz, dated November 7,2022.	10-Q	001-38841	10.5	11/8/2022	
10.26#	Employment Agreement between Precision BioSciences, Inc. and Dr. J. Jefferson Smith, dated November 7, 2022.	10-Q	001-38841	10.6	11/8/2022	
10.27#	Form of Indemnification Agreement between Precision BioSciences, Inc. and its directors and officers.	S-1A	333-230034	10.17	3/18/2019	
10.28#	Non-Employee Director Compensation Plan (as amended).	10-Q	001-38841	10.4	8/8/2022	
10.29#	Executive Employment Agreement, dated September 18, 2021, by and between Michael Amoroso and Precision Biosciences, Inc.	8-K	001-38841	10.1	9/27/2021	
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.					*

Exhibit Number	Description	Form	File No.	Exhibit	Filing Date	Filed Herewith
31.2	Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.					*
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					*
104	Cover Page Interactive Data File (as formatted as Inline XBRL and contained in Exhibit 101)					*

* 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 compensatory 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 9, 2023

By: /s/ Michael Amoroso
Michael Amoroso
President, Chief Executive Officer and Director
(principal executive office and authorized signatory)

Date: March 9, 2023

By: /s/ John Alexander Kelly
John Alexander Kelly
Chief Financial Officer
(principal financial officer)

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/ Michael Amoroso **Michael Amoroso**	President, Chief Executive Officer and Director (*principal executive officer*)	March 9, 2023
/s/ John Alexander Kelly **John Alexander Kelly**	Chief Financial Officer (*principal financial officer*)	March 9, 2023
/s/ Shane Barton **Shane Barton**	Vice President and Corporate Controller (*principal accounting officer)*	March 9, 2023
/s/ Kevin Buehler **Kevin Buehler**	Chair of the Board and Director	March 9, 2023
/s/ Melinda Brown **Melinda Brown**	Director	March 9, 2023
/s/ Stanley Frankel, M.D. **Stanley Frankel, M.D.**	Director	March 9, 2023
/s/ Geno Germano **Geno Germano**	Director	March 9, 2023
/s/ Shari Lisa Piré, J.D. **Shari Lisa Piré, J.D.**	Director	March 9, 2023
/s/ Sam Wadsworth, Ph.D. **Sam Wadsworth, Ph.D.**	Director	March 9, 2023

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, 2022 and 2021, the related consolidated statements of operations, changes in stockholders' equity, and cash flows, for each of the two years in the period ended December 31, 2022, and the related notes (collectively referred to as the "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2022 and 2021, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2022, 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 9, 2023

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, 2022	December 31, 2021
Assets		
Current assets:		
Cash and cash equivalents	$ 189,576	$ 143,663
Accounts receivable	720	488
Prepaid expenses	7,552	17,434
Other current assets	1,257	169
Total current assets	199,105	161,754
Property, equipment, and software—net	20,190	25,154
Intangible assets—net	1,348	2,048
Right-of-use assets—net	2,974	4,180
Investment in equity securities	2,576	3,091
Equity method investment	2,172	3,751
Note receivable—net	7,234	6,879
Other assets	2,570	4,641
Total assets	$ 238,169	$ 211,498
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 1,225	$ 1,144
Accrued compensation	6,259	6,765
Accrued clinical research and development expenses	3,206	4,028
Deferred revenue	46,192	21,244
Lease liabilities	2,037	1,822
Other current liabilities	745	977
Total current liabilities	59,664	35,980
Deferred revenue	82,872	67,015
Lease liabilities	2,776	4,813
Long term debt—net	22,223	2,478
Contract liabilities	10,000	10,000
Other noncurrent liabilities	201	44
Total liabilities	177,736	120,330
Commitments and contingencies (Note 6)		
Stockholders' equity:		
Preferred stock, $0.0001 par value— 10,000,000 shares authorized as of December 31, 2022 and December 31, 2021; no shares issued and outstanding as of December 31, 2022 and December 31, 2021	—	—
Common stock; $0.000005 par value— 200,000,000 shares authorized, 111,774,507 shares issued and 110,964,035 shares outstanding as of December 31, 2022; 61,712,577 shares issued and 60,902,105 shares outstanding as of December 31, 2021	1	—
Additional paid-in capital	489,696	408,795
Accumulated deficit	(428,312)	(316,675)
Treasury stock	(952)	(952)
Total stockholders' equity	60,433	91,168
Total liabilities and stockholders' equity	$ 238,169	$ 211,498

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,	
	2022	2021
Revenue	$ 25,098	$ 115,529
Operating expenses		
Research and development	83,939	115,238
General and administrative	41,525	39,667
Total operating expenses	125,464	154,905
Loss from operations	(100,366)	(39,376)
Other (expense) income, net:		
Impairment charges	(11,438)	—
Loss on disposal of assets	(106)	(26)
(Loss) gain from changes in fair value	(510)	2,555
Gain on deconsolidation of subsidiary	—	5,985
(Loss) income from equity method investment	(1,579)	184
Interest expense	(1,111)	(132)
Interest income	3,473	208
Total other (expense) income, net	(11,271)	8,774
Net loss	$ (111,637)	$ (30,602)
Net loss per share - basic and diluted	$ (1.27)	$ (0.52)
Weighted average shares of common stock outstanding- basic and diluted	87,898,498	58,688,102

See notes to consolidated financial statements

PRECISION BIOSCIENCES, INC.
CONSOLIDATED STATEMENTS OF CHANGES IN STOCKHOLDERS' EQUITY
(In thousands, except share amounts)

	Common Stock		Additional Paid-In Capital	Accumulated Deficit	Treasury Stock	Total Stockholder's Equity
	Shares	Amount				
Balance- December 31, 2020	53,503,124	—	331,450	(286,073)	(952)	44,425
Stock option exercises	1,997,700	—	6,783	—	—	6,783
Issuance of common stock under employee stock purchase plan	126,887	—	804	—	—	804
Share-based compensation expense	—	—	16,514	—	—	16,514
Issuance of common stock to collaboration partners	3,762,190	—	27,739	—	—	27,739
Net proceeds from issuance of common stock	2,322,676	—	25,505	—	—	25,505
Net loss	—	—	—	(30,602)	—	(30,602)
Balance- December 31, 2021	61,712,577	$ —	$ 408,795	$ (316,675)	$ (952)	$ 91,168
Stock option exercises	335,439	—	392	—	—	392
Issuance of common stock under employee stock purchase plan	194,672	1	442	—	—	443
Share-based compensation expense	—	—	19,197	—	—	19,197
Restricted stock units vested	288,323	—	—	—	—	—
Issuance of common stock to collaboration partners	12,407,440	—	11,553	—	—	11,553
Net proceeds from issuance of common stock	36,836,056	—	49,317	—	—	49,317
Net loss	—	$ —	$ —	(111,637)	$ —	(111,637)
Balance- December 31, 2022	111,774,507	1	489,696	(428,312)	(952)	60,433

See notes to consolidated financial statements

PRECISION BIOSCIENCES, INC.
CONSOLIDATED STATEMENTS OF CASH FLOWS
(In thousands)

	For the Years Ended December 31,	
	2022	2021
Cash flows from operating activities:		
Net loss	$ (111,637)	$ (30,602)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	7,798	8,981
Share-based compensation	19,197	16,514
Loss on disposal of assets	106	26
Non-cash interest expense	295	59
Amortization of right-of-use assets	1,206	1,216
Non-cash consideration received from collaboration partners	—	(17,894)
Loss (Gain) on changes in fair value	510	(2,555)
Gain on deconsolidation of subsidiary	—	(5,985)
Loss (Income) from equity method investment	1,579	(184)
Amortization of discount on note receivable	(355)	(13)
Impairment charges	11,438	—
Changes in operating assets and liabilities:		
Prepaid expenses	(962)	5,616
Accounts receivable	(232)	9,512
Other assets and other current assets	1,431	(2,734)
Accounts payable	153	867
Other liabilities and other current liabilities	(1,816)	1,423
Deferred revenue	27,358	(3,164)
Lease liabilities	(1,822)	(1,936)
Contract liabilities	—	10,000
Net cash used in operating activities	(45,753)	(10,853)
Cash flows from investing activities:		
Property, equipment and software	(3,319)	(5,053)
Intangibles assets	—	(750)
Net cash used in investing activities	(3,319)	(5,803)
Cash flows from financing activities:		
Stock option exercises	392	6,783
Employee stock purchase plan	443	804
Issuance of common stock to collaboration partners	25,000	35,000
Offering of common stock, net of issuance costs	49,345	25,477
Issuance of term loan, net of issuance costs	—	2,465
Payments of debt issuance costs	—	(13)
Payment of term loan	—	(2,500)
Borrowings from revolving credit facility, net of issuance costs	19,805	2,505
Net cash provided by financing activities	94,985	70,521
Net increase in cash and cash equivalents	45,913	53,865
Cash and cash equivalents—beginning of period	143,663	89,798
Cash and cash equivalents —end of period	$ 189,576	$ 143,663
Supplemental disclosures of noncash financing and investing activities:		
Property, equipment and software additions included in accounts payable, accrued expenses and other current liabilities	$ 103	$ 103
Cash paid for interest	$ 824	$ 68
Unsettled at-the-market issuances of common stock included in other current assets	$ —	$ 37
Contract liability accrual related to Servier Program Purchase Agreement milestones	$ —	$ 10,000
Non-cash consideration received from collaboration partners	$ —	$ 17,894

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 a clinical stage gene editing company dedicated to improving life by developing *ex vivo* allogeneic CAR T immunotherapies and *in vivo* therapies for genetic and infectious diseases with the application of the Company's wholly owned proprietary ARCUS genome editing platform.

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.

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, estimating services expended by third-party service providers used to recognize research and development expense and determination of the fair value of investments in equity securities.

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.

Certain immaterial amounts from the prior year have been reclassified to conform to current year presentation.

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, 2022 the Company held cash equivalents which are 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. As of December 31, 2021, the Company held an insignificant amount of cash equivalents.

Concentrations of Credit Risk

Financial instruments that potentially subject the Company to concentrations of credit risk consist principally of cash and notes receivable. 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 Lilly and Novartis accounted for 62% and 38% of revenue during the year ended December 31, 2022, respectively. Revenue from Lilly and Servier accounted for 18% and 63% of revenue during the year ended December 31, 2021, respectively. Lilly and Novartis accounted for 58% and 42% of deferred revenue as of December 31, 2022, respectively.

In addition, the Company currently holds a $10.0 million promissory note payable from New Elo (defined below), as described further in Note 12, *Elo Transaction*, which exposes the Company to potential losses in the event of default by New Elo. Counterparty credit risk will be monitored through periodic review of New Elo's financial records. As of December 31, 2022, the Company considers the risk of counterparty default to be minimal.

Property, Equipment and Software

Property, equipment and software ("PP&E") 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 PP&E 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 Charges

Long-lived assets, such as PP&E, intangible assets, and long-term prepaid assets 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.

Fair Value Measurements

Fair value is defined as the price that would be received from selling an asset or paid to transfer a liability in an orderly transaction between market participants at the measurement date. When determining the fair value measurements for assets and liabilities, which are required to be recorded at fair value, we consider the principal or most advantageous market in which we would transact and the market-based risk measurements or assumptions that market participants would use in pricing the asset or liability, such as risks inherent in valuation techniques, transfer restrictions and credit risk. ASC 820, *Fair Value Measurement*, establishes a fair value hierarchy for instruments measured at fair value that distinguishes between assumptions based on market data (observable inputs) and the Company's assumptions (unobservable inputs). Observable inputs are inputs that market participants would use in pricing the asset or liability based on market data obtained from our independent sources. Unobservable inputs are inputs that reflect the Company's assumptions about the inputs that market participants would use in pricing the asset or liability, and are developed based on the best information available in the circumstances. The following fair value hierarchy is used to classify assets and liabilities based on the observable inputs and unobservable inputs used to value the assets and liabilities:

- 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

To the extent that the valuation is based on models or inputs that are less observable or unobservable in the market, the determination of fair value requires more judgment. A financial instrument's level within the fair value hierarchy is based on the lowest level of any input that is significant to the fair value measurement.

Investments in Equity Securities

The Company carries investments in equity securities for which it does not possess the ability to exercise significant influence or control at fair value in the consolidated balance sheets and records changes in fair value in the consolidated statements of operations as a component of other income or expense.

As of December 31, 2022 and December 31, 2021 the Company held common stock in iECURE with a fair value of $2.6 million and $3.1 million, respectively.

Investments under the Equity Method

The Company utilizes the equity method to account for investments when it is determined that the Company possess the ability to exercise significant influence, but not control, over the operating and financial policies of the investee. The ability to exercise significant influence is presumed when the investor possesses more than 20% of the voting interests of the investee. This presumption may be overcome based on specific facts and circumstances that demonstrate that the ability to exercise significant influence is restricted.

In applying the equity method, the Company subsequently increases or decreases the carrying amount of the investment by the Company's proportionate share of the net earnings or losses and other comprehensive income of the investee. In the event that net losses of the investee reduce the carrying amount to zero, additional net losses are recorded if other investments in the investee are at-risk, even if the Company has not committed to provide financial support to the investee.

Leases

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. As the rate implicit in the Company's leases are 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 accounting standards codification ("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.

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, 2022, the Company recorded cumulative catch up adjustments on its contracts with customers that decreased revenue recognition by $5.9 million; the cumulative catch-up adjustments resulted from a change in total estimated effort required to satisfy performance obligations. During the year ended December 31, 2022, the Company recorded $15.4 million in revenue that was included in deferred revenue as of December 31, 2021.

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 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 10, *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 clinical trials and contract manufacturing organizations ("CMOs") engaged to manufacture clinical trial material, costs of licensing technology, and costs of services provided by research and development 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 statements of operations 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 that result from transactions and economic events other than those with stockholders. For the years ended December 31, 2022 and December 31, 2021, there was no difference between net loss and comprehensive loss in the accompanying consolidated statement of operations.

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.

The Company’s diluted net loss per share is the same as basic net loss per share for the years ended December 31, 2022 and December 31, 2021, 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 awards, including stock options, restricted stock units and its employee stock purchase plan, at fair value. Compensation expense is recognized for the Company's share-based compensation awards, net of actual forfeitures, over the requisite service period, which is the vesting period of the respective award.

The fair value of each stock option 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. Expected volatility is estimated based on the historical volatility of the Company

and other comparable publicly traded peer companies. The expected term of the options has been determined utilizing a weighted average 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.

The fair value of each restricted stock unit is determined based on the closing market price of the Company's common stock on the date of grant.

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 Company does not expect the adoption of recent accounting pronouncements not yet adopted will have a material impact on its consolidated financial statements. 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 $1.235 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.

Accounting standards updates issued, but not effective until after December 31, 2022, 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

PP&E consisted of the following as of December 31 (in thousands):

	2022	2021
Construction in progress	$ 533	$ 3,042
Leasehold improvements	22,955	22,784
Software	442	312
Laboratory equipment	23,459	19,291
Office equipment	1,594	1,371
Furniture and fixtures	2,295	2,268
Total property, equipment and software	51,278	49,068
Less accumulated depreciation and amortization	31,088	23,914
Property, equipment and software - net	$ 20,190	$ 25,154

Depreciation expense, including amortization of leasehold improvements and software, was $7.7 million and $8.9 million for the years ended December 31, 2022 and December 31, 2021, respectively.

NOTE 3: INTANGIBLE ASSETS

Intangible assets, net, consisted of the following as of December 31 (in thousands):

	2022	2021
License cost	$ 2,581	$ 2,581
Less: accumulated amortization	(521)	(415)
Less: impairments	(712)	(118)
Intangible assets, net	1,348	2,048

Amortization expense of intangible assets was $0.1 million and less than $0.1 million for the years ended December 31, 2022 and December 31, 2021, respectively. 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 $0.9 million amortized to expense in 2027 and beyond.

NOTE 4: FAIR VALUE MEASUREMENTS

The following represents assets measured at fair value on a recurring basis by the Company (in thousands):

December 31, 2022	Fair Value	Level 1	Level 2	Level 3
Assets:				
Money market funds	$ 868	$ 868	$ —	$ —
Repurchase agreements	40,000	—	40,000	—
Investment in iECURE	2,576	—	—	2,576
	$ 43,444	$ 868	$ 40,000	$ 2,576
Liabilities:				
Final payment fee	$ 199	$ —	$ 199	$ —
	$ 199	$ —	$ 199	$ —

December 31, 2021	Fair Value	Level 1	Level 2	Level 3
Money market funds	$ 12	$ 12	$ —	$ —
Investment in iECURE	3,091	—	—	3,091
	$ 3,103	$ 12	$ —	$ 3,091

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.

Cash Equivalents

As of December 31, 2022, the Company held cash equivalents which are 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. As of December 31, 2021, the Company held an insignificant amount of cash equivalents which were composed of investments in money market funds. The Company classifies investments in money market funds within Level 1 of the fair value hierarchy as the prices are available from quoted prices in active markets. Investments in repurchase agreements are classified within Level 2 of the fair value hierarchy as these instruments are valued using observable market inputs including reported trades, broker/dealer quotes, bids and/or offers.

Investment in iECURE

In August 2021, the Company entered into an Equity Issuance Agreement with iECURE, Inc. ("iECURE"), pursuant to which iECURE issued the Company common stock in iECURE (the "iECURE equity") as additional consideration for a license to use the Company's PCSK9-directed ARCUS nuclease to insert genes into the PCSK9 locus to develop treatments for four pre-specified rare genetic diseases (the "PCSK9 license"). On issuance, the Company accounted for the iECURE equity at fair value under ASC 825, *Financial Instruments* ("ASC 825"). Accordingly, the Company adjusts the carrying value of the iECURE equity to fair value each reporting period with any changes in fair value recorded to other income (expense). During the year ended December 31, 2022, the Company recorded a $0.5 million decrease in the carrying value of its iECURE equity to adjust to fair value as a result of dilution from iECURE's Series A-1 equity raise in such period.

The Company classifies the iECURE equity within Level 3 of the fair value hierarchy as the assessed fair value was based on significant unobservable inputs given iECURE equity is not traded on a public exchange. For additional discussion of accounting for the iECURE Development and License agreement (as defined below) and the iECURE Equity Issuance Agreement (as defined below), refer to Note 10, "Collaboration and License Agreements."

Final Payment Fee

The Company is required to pay a final payment fee upon maturity of the Revolving Line. The final payment fee was determined to be a derivative under ASC 815, therefore these fees were initially measured at fair value and recorded as debt discount to be amortized to interest expense over the term of the Revolving Line. Accordingly, the Company will adjust the carrying value of the final payment fee to fair value each reporting period with any changes in fair value recorded to other income (expense). During the year ended December 31, 2022 adjustments to the carrying value of the final payment fee resulted in less than $0.1 million of income recorded to change in fair value in the consolidated statement of operations.

The Company classifies the final payment fee within Level 2 of the fair value hierarchy as the assessed fair value was based on observable market inputs including the Company's current borrowing rate on the Revolving Line. The final payment fee is included in the other noncurrent liabilities within the consolidated balance sheet as of December 31, 2022.

The following represents a reconciliation of assets measured and carried at fair value on a recurring basis with the use of significant unobservable inputs (Level 3) for the year ended December 31, 2022 (in thousands):

	Investment in iECURE
Balance December 31, 2021	$ 3,091
Acquisitions	—
Losses included in earnings	(515)
Dispositions	—
Balance December 31, 2022	$ 2,576

NOTE 5: DEBT

Elo Loan

In May 2021, the Company's then wholly owned subsidiary, Elo Life Systems, Inc., entered into a loan and security agreement with Pacific Western Bank ("PWB") for a term loan (the "Elo Loan") in the amount of $2.5 million. On December 14, 2021, the Company repaid all outstanding principal and interest on the Elo Loan with proceeds from the Revolving Line (defined below).

Revolving Line

Pursuant to the terms of the loan and security agreement with PWB (as amended from time to time, the "Revolving Line") the Company may request advances on a revolving line of credit of up to an aggregate principal of $30.0 million.

In May 2022, the Company and PWB executed the Seventh Amendment to the Revolving Line (the "Revolving Line Amendment"). Upon the execution of the Revolving Line Amendment, the interest rate on credit advances was modified to the greater of (a) 0.75% above the Prime rate (as defined in the Revolving Line) and (b) 4.25%.

In July 2022, the maturity date of the Revolving Line was extended to June 23, 2024 upon the Company's receipt of $100.0 million in aggregate new gross proceeds (as defined in the Revolving Line Amendment). All outstanding principal amounts under the Revolving Line are due on the maturity date. 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.

In December 2021, the Company borrowed $2.5 million under the Revolving Line to pay all outstanding principal on the Elo Loan. In May 2022, the Company borrowed an additional $20.0 million under the Revolving Line. As of December 31, 2022, $22.5 million was outstanding under the Revolving Line and the unamortized Revolving Line debt discount balance was $0.3 million. As of December 31, 2022, the stated interest rate on the Revolving Line was 8.25% and the effective interest rate was 9.27%.

NOTE 6: 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.

Servier Program Purchase Agreement

On April 9, 2021, the Company entered into a program purchase agreement with Les Laboratoires Servier and Institut de Recherches Internationales Servier (collectively, "Servier"), pursuant to which the Company reacquired all of its global development and commercialization rights previously granted to Servier pursuant to the Development and Commercial License Agreement by and between Servier and the Company, dated February 24, 2016, as amended (the "Servier Agreement"), and mutually terminated the Servier Agreement (the "Program Purchase Agreement").

The Program Purchase Agreement requires the Company to make certain payments to Servier based on the achievement of regulatory and commercial milestones for each product, and a low- to mid-single-digit percentage royalty (subject to certain reductions) based on net sales of approved products, if any, resulting from any continued development and commercialization of the programs by the Company, for a period not to exceed ten years after first commercial sale of the applicable product in the United States or certain countries in Europe. If the Company enters into specified product partnering transactions, the Program Purchase Agreement requires the Company to pay to Servier a portion of certain consideration received pursuant to such product partnering transactions in lieu of the foregoing milestones (with the exception of a one-time clinical phase development milestone) and royalties.

Regulatory and Commercial Milestones

Management assessed the likelihood of each of the regulatory and commercial milestones included in the Program Purchase Agreement in accordance with ASC 450, *Contingencies* ("ASC 450"). If the assessment of a contingency indicates that it is probable that the milestone will be achieved and the amount of the liability can be estimated, then the estimated liability would be accrued in the Company's consolidated balance sheets. Accordingly, a $10.0 million financial contract liability was accrued in the year ended December 31, 2021 and is included in the consolidated balance sheets as of December 31, 2022 and December 31, 2021.

Product Partnering Transaction Consideration Due to Servier

Per the terms of the Program Purchase Agreement, should the Company enter into a product partnering transaction with respect to any of the targets previously nominated by Servier, the Company will pay Servier a percentage of the proceeds received. In accordance with ASC 450, management concluded that the amount of proceeds due to Servier as a result of a future product partnering transaction, if any, cannot be reasonably estimated as of the date of this Annual Report on Form 10-K. As such, no contingency for this provision was included in the consolidated financial statements as of December 31, 2022 or December 31, 2021.

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. The Company has existing leases that include variable lease payments that are not included in the right-of-use assets 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:

	For the Years Ended December 31,	
(in thousands)	**2022**	**2021**
Lease Cost		
Operating lease cost	$ 1,644	$ 1,951
Short-term lease cost	563	342
Variable lease cost	746	1,131
Total Lease Cost	$ 2,953	$ 3,424
Other Information		
Operating cash flows used for operating leases	2,264	2,649
Operating lease liabilities arising from obtaining right-of-use assets	—	—
Operating Leases		
Weighted average remaining lease term (in years)	2.9	3.7
Operating Leases		
Weighted average discount rate	7.7%	7.8%

Future lease payments under non-cancelable operating leases with terms of greater than one year as of December 31, 2022, were as follows:

(in thousands)	**December 31, 2022**
2023	$ 2,323
2024	1,594
2025	529
2026	545
2027	372
Total lease payments	5,363
Less: imputed interest	550
Total operating lease liabilities	$ 4,813

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 7: STOCKHOLDERS' EQUITY

Capital Structure

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 8: 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, 2022 there were 1,932,584 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 2019 Plan had 8,841,134 stock options and 3,419,830 restricted stock units ("RSUs") outstanding as of December 31, 2022.

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 December 31, 2022, the aggregate number of shares available for issuance under the 2019 Plan has been increased by 6,589,999 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, 2022, 231,039 shares were available to be issued under the 2019 Plan.

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 December 31, 2022, the aggregate number of shares available for issuance under the 2019 ESPP has been increased by 1,647,499 shares pursuant to this provision. 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, 2022, we had issued 447,787 shares under the 2019 ESPP. As of December 31, 2022, 1,724,712 shares were available to be issued under the 2019 ESPP. The Company recognized share-based compensation expense related to the ESPP of $0.2 million and $0.3 million during the years ended December 31, 2022 and December 31, 2021, respectively.

On August 9, 2021, the Company's board of directors approved the adoption of the Precision BioSciences, Inc. 2021 Employment Inducement Incentive Award Plan (as amended, the "Inducement Award Plan").

The Inducement Award Plan provides for the grant of non-qualified stock options, stock appreciation rights, restricted stock, RSUs and other share-based awards to newly hired employees who have not previously been an employee or member of the board, or an employee who is being rehired following a bona fide period of non-employment by the Company. No more than 9,000,000 shares of the Company's common stock may be issued under the Inducement Award Plan. As of December 31, 2022, 5,827,204 shares were available to be issued under the Inducement Award Plan. The Inducement Award Plan had 2,949,134 stock options and 199,454 RSUs outstanding as of December 31, 2022.

The Company recorded employee and nonemployee share-based compensation expense as follows (in thousands):

	Years Ended December 31,	
	2022	2021
Employee	$ 15,921	$ 14,963
Nonemployee	3,276	1,551
	$ 19,197	$ 16,514

Share-based compensation expense is included in the following line items in the consolidated statements of operations (in thousands):

	Years Ended December 31,	
	2022	2021
Research and development	$ 7,973	$ 9,101
General and administrative	11,224	7,413
	$ 19,197	$ 16,514

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,	
	2022	2021
Estimated dividend yield	0.00%	0.00%
Weighted-average expected stock price volatility	79.66%	73.02%
Weighted-average risk-free interest rate	2.57%	1.07%
Expected term of options (in years)	6.07	6.25
Weighted-average fair value per option	$ 1.86	$ 6.91

The expected volatility rates are estimated based on the actual volatility of a peer group comprising the Company and other comparable public companies over the expected term. The expected term represents the average time that stock options 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 at the time of grant for the expected term of the option.

The following table summarizes activity in the Company's stock option plans for the years ended December 31, 2021 and December 31, 2022 :

	Outstanding Option Shares	Weighted-Average Exercise Price
Balance as of December 31, 2020	10,544,270	7.88
Granted	2,831,025	10.62
Exercised	(1,997,700)	3.40
Forfeited/canceled	(1,457,281)	9.84
Balance as of December 31, 2021	9,920,314	9.28
Granted	6,713,764	2.69
Exercised	(335,439)	1.17
Forfeited/canceled	(2,575,787)	8.66
Balance as of December 31, 2022	13,722,852	6.37

The intrinsic value of stock options exercised was $0.7 million and $15.5 million during the years ended December 31, 2022 and December 31, 2021, respectively.

During the year ended December 31, 2022, the Company granted 3,327,107 RSUs with a grant date fair value of $8.7 million. The fair value of the RSUs will be recognized as expense over the requisite vesting period.

The following table summarizes the Company's RSU activity for the years ended December 31, 2021 and December 31, 2022:

	RSU Awards	Weighted-Average Grant Date Fair Value
Unvested RSUs as of December 31, 2020	—	—
Granted	849,780	11.30
Forfeited	(76,277)	11.34
Vested	—	—
Unvested RSUs as of December 31, 2021	773,503	11.29
Granted	3,327,107	2.62
Forfeited	(193,003)	7.14
Vested	(288,323)	11.21
Unvested RSUs As of December 31, 2022	3,619,284	3.55

There was approximately $31.5 million of total unrecognized compensation cost related to unvested stock options and RSUs as of December 31, 2022, which is expected to be recognized over a weighted-average period of 2.4 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, 2022 and December 31, 2021.

Years Ended December 31,		Number of Options	Weighted-Average Remaining Contractual Life (in years)		Weighted-Average Exercise Price
2022	Expected to be exercisable	13,722,852	7.77	$	6.37
2022	Currently exercisable	5,289,519	5.84	$	9.19
2021	Expected to be exercisable	9,920,314	7.47	$	9.28
2021	Currently exercisable	4,840,006	6.09	$	8.83

The following table summarizes certain information about stock options outstanding under the stock option plans for the years ended December 31, 2022 and December 31, 2021, respectively:

Year Ended December 31, 2022			
Exercise price	Number of Options Outstanding	Weighted- Average Remaining Life	Number of Options Exercisable
$0.02 - $1.55	2,027,527	7.82	616,558
$1.68 - $3.34	2,441,283	9.35	5,842
$4.08 - $4.56	2,219,603	9.07	1,424
$5.67 - $9.69	3,529,976	6.98	2,095,318
$10.17 - $16.00	3,504,463	6.61	2,570,377
	13,722,852		5,289,519

Year Ended December 31, 2021			
Exercise price	Number of Options Outstanding	Weighted- Average Remaining Life	Number of Options Exercisable
$0.02 - $1.20	878,460	4.28	878,460
$5.67-$6.31	1,330,901	8.18	477,574
$6.45 - $9.79	3,025,794	8.56	1,010,298
$10.17-$12.52	2,828,331	7.36	1,237,568
$12.60-$16.00	1,856,828	6.88	1,236,106
	9,920,314		4,840,006

NOTE 9: 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, 2022 and December 31, 2021.

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 $0.9 million and $1.0 million to the Retirement Plan during the years ended December 31, 2022 and December 31, 2021, 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 10: COLLABORATION AND LICENSE AGREEMENTS

Collaboration and License Agreement with Novartis

On June 14, 2022, the Company entered into a collaboration and license agreement (the "Novartis Agreement") with Novartis Pharma AG ("Novartis"), which became effective on June 15, 2022 (the "Novartis Effective Date"), to collaborate to discover and develop *in vivo* gene editing products incorporating our custom ARCUS nucleases for the purpose of seeking to research and develop potential treatments for certain diseases (as defined in the Novartis Agreement, the "Licensed Products"). Any initial Licensed Products will be developed for the potential treatment of certain hemoglobinopathies, including sickle cell disease and beta thalassemia.

Pursuant to the terms of the Novartis Agreement, the Company will develop an ARCUS nuclease and conduct *in vitro* characterization for the Licensed Products, with Novartis then assuming responsibility for all subsequent development, manufacturing and commercialization activities. Novartis will receive an exclusive license for, and be required to use commercially reasonable efforts to conduct all subsequent research, development, manufacture and commercialization activities with respect to the Licensed Products. The Company will initially develop a single, custom ARCUS nuclease for a defined "safe harbor" target site for insertion of specified therapeutic payloads in the patient's genome (the "Initial Nuclease") for Novartis to further develop as a potential *in vivo* treatment option for certain hemoglobinopathies, including sickle cell disease and beta thalassemia. Pursuant to the terms of the Novartis Agreement, Novartis may elect, subject to payment of a fee to the Company, to replace Licensed Products based on the Initial Nuclease with Licensed Products based on a second custom ARCUS nuclease the Company designs for gene editing of a specified human gene target associated with hemoglobinopathies (the "Replacement Nuclease"). Additionally, Novartis has the option, upon payment of a fee to the Company for each exercise of the option, to include Licensed Products utilizing the Initial Nuclease for insertion of up to three additional specified therapeutic payloads at the "safe harbor" target site, each intended to treat a particular genetic disease. The exercise period for such option ends on the earlier of (a) the fourth anniversary of the Novartis Effective Date and (b) the replacement of the Initial Nuclease with the Replacement Nuclease as described above.

In July 2022, the Company received a $50.0 million upfront cash payment under the Novartis Agreement. Additionally, on the Novartis Effective Date, Novartis made an equity investment in the Company's common stock pursuant to a stock purchase agreement (the "Novartis Stock Purchase Agreement") pursuant to which, on the Novartis Effective Date, the Company issued and sold to Novartis 12,407,440 shares of the Company's common stock (the "Novartis Shares") in a private placement transaction for an aggregate purchase price of $25.0 million, or approximately $2.01 per share. The price per share of the Company's common stock under the Novartis Stock Purchase Agreement represented a 20% premium over the volume-weighted-average-price of the Company's common stock over the 10 trading days preceding the execution date of the Novartis Stock Purchase Agreement. Management concluded that the Novartis Stock Purchase Agreement was to be combined with the Novartis Agreement for accounting purposes. Of the total $75.0 million upfront compensation, the Company applied equity accounting guidance to measure the $11.6 million recorded in equity upon the issuance of the shares, and $63.4 million was identified as transaction price allocated to the revenue arrangement.

Pursuant to the Novartis Stock Purchase Agreement, subject to certain exceptions, Novartis may not sell the Novartis Shares without the Company's approval for a period of two years following the Novartis Effective Date. In addition, for a period of two years following the Novartis Effective Date, Novartis and its affiliates may not (a) effect or otherwise participate in, directly or indirectly, any acquisition of any of our securities or material assets, any tender offer or exchange offer, merger or other business combination or change of control involving the Company, any recapitalization, restructuring, liquidation, dissolution or other extraordinary transaction with respect to the Company, or any solicitation of proxies or consents to vote any of the Company's securities or (b) act with any other person, or publicly disclose any intention, to do any of the foregoing. The Novartis Stock Purchase Agreement also contains customary representations, warranties, and covenants of both parties.

On the Novartis Effective Date, the Company and Novartis also entered into a registration rights agreement (the "Registration Rights Agreement") pursuant to which the Company has agreed, within the time periods specified in the Registration Rights Agreement, to register the resale of the Novartis Shares on a registration statement to be filed with the SEC. The Registration Rights Agreement contains customary indemnification provisions, and all registration rights terminate in their entirety effective on the first date on which there cease to be any Registrable Securities (as defined in the Registration Rights Agreement) outstanding.

The Company will also be eligible to receive milestone payments of up to an aggregate of approximately $1.4 billion as well as 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 to low-double digit percentages on net sales of Licensed Products, subject to customary potential reductions. Novartis'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 the first commercial sale of the Licensed Product.

Unless earlier terminated, the Novartis 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. Novartis has the right to terminate the Novartis Agreement without cause by providing advance notice to the Company. Either party may terminate the Novartis Agreement for material breach by the other party and a failure to cure such breach within the time period specified in the Novartis Agreement. The Company may also terminate the Novartis Agreement in the event that Novartis brings a challenge to our patents.

The Company assessed the Novartis Agreement 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 targets are not distinct because they are all based on the ARCUS proprietary genome editing platform. The Company has concluded that the agreement with Novartis contains the following promises: (i) license of intellectual property; (ii) performance of research and development ("R&D") services, and (iii) Joint Steering Committee ("JSC") participation. The Company determined that the license of intellectual property and R&D services were not distinct from each other, as the license and R&D services are highly interdependent upon one another. The JSC participation was determined to be an immaterial promise as the time commitment and related cost associated with performance of JSC participation is expected to be inconsequential to the total consideration in the contract. As such, the Company determined that these promises should be combined into a single performance obligation.

The Company recognizes revenue from the $50.0 million upfront cash payment, $13.4 million allocated to the transaction price from the Novartis Stock Purchase Agreement, and variable consideration 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 hours of research work performed relative to expected hours of research work to be incurred in the future to satisfy the performance obligation. Management will evaluate and adjust the total expected research effort for the performance obligation on a quarterly basis based upon actual research hours incurred to date relative to research hour forecasts. 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.

During the year ended December 31, 2022, the Company recognized revenue under the Novartis Agreement of $9.5 million. Deferred revenue related to the Novartis Agreement amounted to $54.2 million as of December 31, 2022, of which $27.9 million, was included in current liabilities within the consolidated balance sheets.

Development and License Agreement with Eli Lilly

On November 19, 2020, the Company entered into a development and license agreement, subsequently amended by the First Amendment to the Development and License Agreement dated August 9, 2021 (as amended, the "Lilly Agreement") with Eli Lilly and Company ("Lilly") to collaborate to discover and develop *in vivo* gene editing products incorporating the Company's ARCUS nucleases to utilize ARCUS for the research and development of potential *in vivo* therapies for genetic disorders. Lilly has initially nominated Duchenne muscular dystrophy, a liver-directed target and a central nervous system directed target. Under the terms of the Development and License Agreement, Lilly has the right to nominate up to three additional gene targets for genetic disorders over the initial nomination period of four years. 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. Additionally, under the terms of the Lilly Agreement, Lilly has the option to replace up to two gene targets upon Lilly's election and payment of a replacement target fee. Under the terms of the Lilly Agreement, Lilly received 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 Lilly Agreement provides that the Company will be responsible for conducting certain pre-clinical research and investigational new drug application ("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.

In connection with the closing of the Lilly Agreement on January 6, 2021, the Company received an upfront cash payment of $100.0 million. 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. Simultaneously with the entry into the Lilly Agreement, the Company and Lilly entered into a Share Purchase Agreement (the "Lilly Share Purchase Agreement"), pursuant to which Lilly purchased 3,762,190 shares of the Company's common stock for a purchase price of $35.0 million. Management concluded that the Lilly Share Purchase Agreement was to be combined with the Lilly Agreement for accounting purposes. Of the total $135.0 million upfront compensation, the Company applied equity accounting guidance to measure the $27.7 million recorded in equity upon the issuance of the shares, and $107.3 million was identified as the transaction price allocated to the revenue arrangement.

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 targets are not distinct because they are all based on the ARCUS proprietary genome editing platform. The Company has concluded that the agreement with Lilly contains the following promises: (i) license of intellectual property; (ii) performance of R&D services, (iii) the manufacture of pre-clinical supply, (iv) JSC Participation, and (v) regulatory responsibilities. The Company determined that the license of intellectual property, R&D services, manufacture of pre-clinical development material, and regulatory responsibilities were not distinct from each other, as the license, R&D services, pre-clinical supply, and regulatory responsibilities are highly interdependent upon one another. The JSC participation was determined to be an immaterial promise as the time commitment and related cost associated with performance of JSC participation is expected to be inconsequential to the total consideration in the contract. As such, the Company determined that these promises should be combined into a single performance obligation.

The Company recognizes revenue from the $100.0 million upfront cash payment, $7.3 million allocated to the transaction price from the Lilly Share Purchase Agreement, and variable consideration 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 progress to date relative to research progress forecasts. 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.

During the years ended December 31, 2022 and 2021, the Company recognized revenue under the Lilly Agreement of $15.6 million and $21.0 million, respectively. Deferred revenue related to the Lilly Agreement amounted to $74.8 million and $88.3 million as of December 31, 2022 and December 31, 2021, respectively, of which $18.3 million and $21.2 million, respectively, was included in current liabilities within the consolidated balance sheets.

Development and License Agreement with iECURE

In August 2021, the Company entered into a development and license agreement with iECURE (the "iECURE Development and License Agreement") under which iECURE was to advance the Company's PBGENE-PCSK9 candidate through the Phase 1 clinical trial in order to gain access to Precision's PCSK9-directed ARCUS nuclease to develop four other pre-specified gene editing therapies for rare genetic diseases (the "iECURE Agreement"). In conjunction with the iECURE Agreement, the Company also granted iECURE a license to use its PCSK9-directed ARCUS nuclease to insert genes into the PCSK9 locus to develop treatments for four other pre-specified rare genetic diseases, including ornithine transcarbamylase ("OTC") deficiency, Citrullinemia Type 1 ("CTLN1"), Phenylketonuria ("PKU"), and another program focused on liver disease. Simultaneously with the entry into the iECURE Agreement, the Company and iECURE entered into an Equity Issuance Agreement (the "iECURE Equity Issuance Agreement"), pursuant to which iECURE issued the Company common stock in iECURE as additional consideration for the PCSK9 license. Management concluded that the iECURE Equity Issuance Agreement was to be combined with the iECURE Development and License Agreement (together, the "iECURE Agreements") for accounting purposes. Additionally, the Company is eligible to receive milestone and mid-single digit to low double digit royalty payments on sales of iECURE products developed with ARCUS.

The fair value of the iECURE equity at inception of the iECURE agreements was assessed to be $0.5 million and was initially recorded to the investment in equity securities line item of the consolidated balance sheets. As further discussed in Note 4, *Fair Value Measurements*, on issuance, Management elected to account for the iECURE equity at fair value under ASC 825. Accordingly, the Company adjusts the carrying value of the iECURE equity to fair value each reporting period with any changes in fair value recorded to other income (expense). During the year ended December 31, 2022, the Company recorded a $0.5 million decrease in the carrying value of its iECURE equity to adjust to fair value as a result of dilution from iECURE's Series A-1 equity raise in such period. The fair value of the costs to be incurred by iECURE to progress the Company's PBGENE-PCSK9 candidate through the Phase 1 clinical trial (the "PCSK9 Prepaid") was assessed to be $17.4 million and was recorded to the prepaid expenses and other assets line items of the consolidated balance sheets. The PCSK9 Prepaid was amortized to research and development expense on a pro-rata basis as iECURE incurred costs to progress the PBGENE-PCSK9 candidate through the Phase 1 clinical trial.

As further discussed in Note 11, *Impairment Charges,* the remaining unamortized PCSK9 Prepaid was fully impaired during the year ended December 31, 2022 as the Company made the decision to cease pursuit of PBGENE-PCSK9 for FH with iECURE as its partner. Accordingly, there was no PCSK9 Prepaid balance as of December 31, 2022. As of December 31, 2021, the remaining balance of the PCSK9 Prepaid was $13.0 million, which was included in the prepaid expenses and other assets line items of the consolidated balance sheets in the amounts of $10.4 million and $2.6 million, respectively.

During the year ended December 31, 2022, the Company recognized no revenue under the iECURE agreements. During the year ended December 31, 2021, the Company recognized $17.9 million of revenue under the iECURE agreements. During the years ended December 31, 2022 and 2021, the Company recognized $2.1 million and $4.4 million of research and development expense related to amortization of the PCSK9 Prepaid.

Development and Commercial License Agreement with Servier

The Company has developed certain allogeneic CAR T candidates, including PBCAR0191 and the stealth cell PBCAR19B, each targeting CD19, as well as four additional product targets under the Servier Agreement. Pursuant to the terms of the Program Purchase Agreement, the Company regained full global rights to research, develop, manufacture and commercialize products resulting from such programs, with sole control over all activities. Additionally, per the terms of the Program Purchase Agreement the Company does not have an obligation to continue development of the four additional product targets under the Servier Agreement. With respect to products directed to CD19, Servier has certain rights of negotiation, which may be exercised during a specified time period if the Company elects to initiate a process or entertain third party offers for partnering such products.

Pursuant to the terms of the Program Purchase Agreement, the Company made a payment of $1.25 million in cash to Servier and agreed to waive earned milestones totaling $18.75 million that would have been otherwise payable to the Company. The Program Purchase Agreement also requires the Company to make certain payments to Servier based on the achievement of regulatory and commercial milestones for each product, and a low- to mid-single-digit percentage royalty (subject to certain reductions) based on net sales of approved products, if any, resulting from any continued development and commercialization of the programs by the Company, for a period not to exceed ten years after first commercial sale of the applicable product in the United States or certain countries in Europe. If the Company enters into specified product partnering transactions, the Program Purchase Agreement requires the Company to pay to Servier a portion of certain consideration received pursuant to such product partnering transactions in lieu of the foregoing milestones (with the exception of a one-time clinical phase development milestone) and royalties. For additional discussion of accounting for payment obligations arising from the Program Purchase Agreement, refer to Note 6, *Commitments and Contingencies*.

The Company did not recognize any revenue under the Servier Agreement during the year ended December 31, 2022. During the year ended December 31, 2021, the Company recognized revenue under the Servier Agreement of approximately $72.9 million. The Company did not have deferred revenue related to the Servier Agreement as of December 31, 2022 or December 31, 2021.

NOTE 11: IMPAIRMENT CHARGES

During the twelve months ended December 31, 2022, the Company recorded impairment charges of $10.8 million related to the PCSK9 Prepaid as the Company made the decision to cease pursuit of PBGENE-PCSK9 for FH with iECURE as its partner. The impairment charge represents the remaining unamortized balance of the PCSK9 Prepaid.

During the twelve months ended December 31, 2022, the Company recorded intangible asset impairment charges of $0.6 million related to licensed technology rights that are no longer in use. As these licensed technology rights are no longer in use by the Company, the impairment charge represents the remaining unamortized balance of the intangibles.

NOTE 12: ELO TRANSACTION

In December 2021, the Company and its then wholly owned subsidiary, Elo Life Systems, Inc., entered into an agreement with a syndicate of investors, pursuant to which the Company contributed substantially all of the assets of Elo Life Systems, Inc. to a newly formed entity (the “Elo Transaction”). In connection with the Elo Transaction, the Company granted the newly formed entity ("New Elo") an exclusive license to certain of the Company’s intellectual property for use in non-medical applications with respect to plants, farm animals and certain other organisms. In addition, all of the Company’s employees in its former food segment, including its management, became employees of New Elo.

Investment in New Elo

As partial consideration for the assets contributed and license granted by the Company to New Elo, the Company received Common Stock in New Elo. Upon the closing of the Elo Transaction, the Company owned approximately 55% of New Elo's voting shares. It was determined that the noncontrolling shareholders of New Elo have substantive rights to participate in the financial and operating decisions of New Elo. As such, it was determined that the Company does not possess control over New Elo or have significant decision-making authority. Accordingly, New Elo was not consolidated in the Company's financial statements. However, it was determined that the Company possesses the ability to exercise significant influence over the operating and financial policies of New Elo. As such, the Company accounts for its investment in New Elo under the equity method.

In the year ended December 31, 2022, New Elo issued additional shares to a syndicate of investors (the "New Elo Issuance") that diluted the Company's ownership to 37% of New Elo's voting shares. Prior to the New Elo Issuance, the Company's Investment in New Elo had no carrying value as the cumulative proportionate share of New Elo's net loss exceeded the initial carrying value of the Investment in New Elo. Accordingly, the Company recorded a gain of $4.7 million in the year ended December 31, 2022 as a result of the increase in the Company's proportionate share of New Elo's net assets.

The Company's proportionate share of New Elo's net loss for the year ended December 31, 2022 was $6.3 million. The Company's proportionate share of New Elo's net income for the year ended December 31, 2021 was $0.2 million.

The following represents a reconciliation of the Company's Investment in New Elo for the year ended December 31, 2022:

(in thousands)	**Investment in New Elo**
Balance as of December 31, 2021	$ 3,751
Gain from New Elo Issuance	4,743
Proportionate share of New Elo losses	(6,322)
Balance as of December 31, 2022	**$ 2,172**

Note Receivable

As partial consideration for the assets contributed and license granted by the Company to New Elo, the Company received a $10.0 million promissory note payable from New Elo (the "Note Receivable"). The Note Receivable matures on the earlier of (i) December 1, 2028 or (ii) a Deemed Liquidation Event (as defined in the New Elo's Amended and Restated Certificate of Incorporation). The Note accrues interest at 2.00% per annum and is payable annually in December.

As of December 31, 2022, the carrying value of the Note Receivable was $7.2 million. The $2.8 million discount on the Note Receivable will be amortized to interest income over the life of the Note.

Gain on Deconsolidation of Subsidiary

The $6.0 million gain on deconsolidation of subsidiary recorded in the year ended December 31, 2021 was determined based on the difference between the $4.4 million book value of the net assets that the Company contributed to New Elo and the $10.4 million combined fair value of the Note and the Company's ownership in New Elo as of December 17, 2021.

NOTE 13: INCOME TAXES

The Company recorded no federal or state income tax expense and due to the operating losses incurred for the years ended December 31, 2022 and December 31, 2021.

Significant components of the Company's deferred tax assets and deferred tax liabilities are as follows (in thousands):

	Years Ended December 31,	
	2022	2021
Noncurrent deferred tax assets:		
Net operating loss carryforwards	$ 36,457	$ 41,162
Contribution carryforwards	48	48
Lease liability	1,120	1,526
Deferred revenue	30,022	20,294
Capitalized R&D costs	15,893	—
Other assets	14,279	11,647
Tax credits	24,721	20,942
Less: valuation allowance	(121,372)	(94,071)
Total deferred tax assets, noncurrent	1,168	1,548
Noncurrent deferred tax liability:		
Investments and other	476	587
Right of use asset	692	961
Total deferred tax liabilities, noncurrent	1,168	1,548
Net deferred tax assets	$ —	$ —

As of December 31, 2022 and December 31, 2021, 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, 2022 of $27.3 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 ("NOL") carryforwards for the year.

The reasons for the difference between actual income tax benefit for the years ended December 31, 2022 and December 31, 2021 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, 2022		Year Ended December 31, 2021	
	Amount	% of Pre-Tax Loss	Amount	% of Pre-Tax Loss
Income tax expense at statutory rate	$ (23,444)	21.0%	$ (6,677)	21.8%
State income taxes, net of federal tax benefit	(250)	0.2%	(634)	2.1%
Non-deductible expenses	33	0.0%	121	(0.4%)
Stock compensation - nondeductible	599	(0.5%)	(2,094)	6.8%
Stock compensation - forfeitures	2,233	(2.0%)	—	0.0%
R&D and orphan drug credits	(3,790)	3.4%	(5,239)	17.1%
Other	314	(0.3%)	567	(1.9%)
Change in state tax rate	(3,004)	2.7%	(843)	2.8%
Change in valuation allowance	27,309	(24.5%)	14,799	(48.3%)
Income tax (benefit) expense	$ —	0.0%	$ —	0.0%

As of December 31, 2022, the Company had federal and state NOL carryforwards of approximately $159.5 million and $119.1 million respectively. As of December 31, 2021, the Company had federal, state, and foreign NOL carryforwards of approximately $181.0 million, $122.2 million, and $0.4 million, respectively. The tax benefit recognized in 2022 related to NOL carryforwards was approximately $4.4 million.

The federal NOL carryforward million carries forward indefinitely. The state NOL carryforwards begin to expire in 2027. As of December 31, 2022, the Company had federal and state R&D tax credits of $13.2 million and an amount less than $0.1 million, which begin to expire in 2027 and 2030, respectively. As of December 31, 2021, the Company had federal and state tax R&D credits of $11.4 million and an amount less than $0.1 million. As of December 31, 2022 and December 31, 2021, the Company had federal

Orphan Drug credits of $11.6 million and $9.5 million, respectively, which begin to expire in 2038. As of December 31, 2022 and December 31, 2021, the Company had federal contribution carryforwards of $0.2 million which began to expire in 2022.

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, 2022 and December 31, 2021, 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, 2022 and December 31, 2021, the Company had no such accruals.

In November 2021, North Carolina enacted the 2021 Appropriations Act, which included a gradual corporate income tax rate decrease from the current 2.5% to 0% by 2030. Due to the uncertainty of projecting income through 2030, the Company calculated, before consideration of the valuation allowance, its North Carolina net operating losses using the current 2.5% rate which is in effect through 2024. The Company will continue to monitor its future North Carolina taxable income and its ability to utilize its deferred tax asset for its net operating loss carryover. If the Company does not become profitable in North Carolina prior to 2025, or it becomes more certain that the Company will not be able to utilize its North Carolina net operating losses before the tax rate drops to 0%, the Company will then remeasure its deferred tax asset at that time.

The TCJA 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, 2021 or December 31, 2021 and therefore, no GILTI tax has been recorded for the years then ended.

NOTE 14: 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 of inclusion 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.

	Years Ended December 31,	
	2022	2021
Net loss (in thousands)	$ (111,637)	$ (30,602)
Weighted average shares outstanding - basic and diluted	87,898,498	58,688,102
Net loss per share - basic and diluted	(1.27)	(0.52)

The following weighted-average common stock equivalents were excluded from the calculation of diluted loss per share because their inclusion would have been anti-dilutive:

	Years Ended December 31,	
	2022	2021
Unvested Restricted Stock Units	2,199,013	430,026
Stock Options	2,376,666	4,626,930
Unsettled ESPP Contributions	61,337	12,550
Total common stock equivalents excluded from diluted net loss per share	4,637,016	5,069,506

NOTE 15: SEGMENT REPORTING

The Company has determined that the Chief Executive Officer ("CEO") is the Company's chief operating decision maker ("CODM") as the CEO makes decisions as it relates to allocation of resources and key market strategies. The CODM reviews financial information presented on a consolidated basis. Additionally, resource allocation and key market strategy decisions are made by the CODM based on consolidated results. As such, it was concluded that the Company operates as one segment.

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Executive Officers

Michael Amoroso
President, Chief Executive Officer and Director

Alex Kelly
Chief Financial Officer

Alan List, M.D.
Chief Medical Officer

Dario Scimeca
General Counsel and Secretary

Jeff Smith, Ph.D.
Chief Research Officer

Board of Directors

Kevin J. Buehler
Chair of the Board,
Former Division Head, Alcon Laboratories Inc.

Michael Amoroso
President, Chief Executive Officer and Director

Melinda Brown
Chief Financial Officer, The Draft Network

Stanley R. Frankel, M.D.
Former Chief Medical Officer, Cytovia Therapeutics, Inc.

Geno Germano
President and Chief Executive Officer, Elucida Oncology, Inc.

Shari Lisa Piré
Chief Legal & Sustainability Officer, Plume Design, Inc.

Samuel Wadsworth, Ph.D.
Senior Scientific Advisor, Ultragenyx Pharmaceutical Inc.

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Annual Meeting of Stockholders
Thursday, May 4, 2023
11:00 a.m., Eastern Time
Via live webcast

Common Stock Listing
Nasdaq: DTIL

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