

Fiscal Year  
**2023**  
**ANNUAL**  
**REPORT**



**PRECISION**  
BIOSCIENCES

This letter contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, including statements regarding the Company's planned strategy, business focus and intended product development. The reader is cautioned not to rely on these statements, which are based on current expectations of future events. 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. For important information about these statements, including further descriptions of the important risks, uncertainties and other factors that could cause actual results to differ materially from expectations or projections expressed in any forward-looking statements, please see the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2023 under the captions "Risk Factor Summary" and "Item 1A. Risk Factors." Such factors may be updated from time to time in the Company's other filings with the SEC. Precision BioSciences, Inc. does not plan to publicly update or revise any such forward-looking statements, whether as a result of any new information, future events or developments, changed circumstances or otherwise, except as may be required by applicable law.

Dear Shareholders:

Since our founding, we have maintained steadfast dedication to improve life for patients in need by translating the immense potential of genome editing into curative therapeutic solutions. **In my last letter, I said we expected 2023 would be a transformative year for Precision. It was.**

The prolonged decline of financial markets for small cap biotech stocks was our reality in much of 2023 following a difficult 2022. Our share price suffered due to a declining biotechnology market resulting in a lower valuation of the company. Amidst these difficult conditions, we held thoughtful strategic discussions with our board, investors, and advisors and determined that we could not adequately fund both a cancer cell therapy business and an *in vivo* gene editing business, so we made hard choices in order to create future shareholder and societal value.

**In 2023, we made the strategic decision to transform our company by solely focusing our energy and our capital on *in vivo* gene editing.** It was a carefully considered decision because it involved divesting clinical stage blood cancer cell therapy programs and reducing our operating footprint to make greater investments in our core capability – *in vivo* gene editing. We believe it was and is absolutely the right decision for Precision BioSciences, our shareholders, and the patients who we want to ultimately benefit from the work we do every day.

**Underlying this shift is our confidence that our proprietary ARCUS genome editing platform**, which was invented by Precision scientists, is our greatest asset and is **uniquely suited for differentiated gene editing applications due to its cut type, its small size, and its simplicity.** We believe the differentiated capabilities of ARCUS will enable us to help people who have incurable genetic diseases and chronic life-limiting infectious diseases, such as in our lead wholly owned program for chronic hepatitis B virus.

**We made two critical decisions in 2023 to accelerate investment in our *in vivo* gene editing portfolio.**

- **First, we amended our agreement with Prevail Therapeutics** to shift some pre-clinical work to our partner in order to focus the Precision team's efforts on our own *in vivo* gene editing programs.
- **Second, we systematically monetized our cell therapy assets to fund *in vivo* gene editing programs.** We began by divesting azercabtagene zapreleucel (azer-cel), our clinical stage allogeneic CAR T therapy, to Imugene for cancer rights along with our CAR T infrastructure and cell therapy teams. Subsequently, we licensed azer-cel for autoimmune diseases and other indications outside of cancer to TG Therapeutics, a commercial stage partner. Finally, we granted a non-exclusive license to one of our foundational cell therapy methodology patents to Caribou Biosciences. In total, these three transactions raised approximately \$50 million in cash and potential near-term milestones to extend our cash runway while placing our cell therapy assets in the hands of capable partners.

To further showcase the potential of ARCUS, we conducted an *in vivo* gene editing R&D Day to highlight how ARCUS' cut, size, and simplicity allow Precision to focus on diseases that require more sophisticated gene editing

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capabilities such as gene insertion (inserting a gene to add function), gene elimination (removing an entire genome such as a viral genome), and gene excision (removing a large portion of a genome).

- **PBGENE-HBV** (viral DNA elimination program) - **We are developing PBGENE-HBV as a potential treatment for people with chronic hepatitis B, a disease that affects approximately 300 million people worldwide.** We have designed this drug to eliminate all sources of the virus, including both the cccDNA and viral genomes that are integrated into human liver cells. Preclinical data demonstrated strong proof-of-concept efficacy and safety for PBGENE-HBV. In early 2024, we received pre-Investigational New Drug (IND) regulatory feedback from the U.S. FDA and from agencies outside the U.S. that provided clarity and alignment on IND- and clinical trial application (CTA)-enabling preclinical plans and clinical strategy. Our team is focused on completing these activities and we expect to submit an IND and/or CTA for this program in 2024.
  - **PBGENE-PMM** (mutant mitochondrial DNA elimination program) - **PBGENE-PMM is a first of its kind potential treatment for m.3243-associated primary mitochondrial myopathy (PMM) by targeting mutant mitochondrial DNA.** Mitochondrial diseases are the most common hereditary metabolic disorder in the world. The m.3243 associated primary mitochondrial myopathy that our program intends to address is sizable, affecting up to 25,000 people in the U.S. alone. We published new preclinical data in *Nature Metabolism* highlighting the high specificity of ARCUS nucleases to edit and eliminate mutant mitochondrial DNA while allowing wild-type (normal) mitochondrial DNA to repopulate in the mitochondria, thus improving normal function. This is an exciting program because ARCUS nucleases are able to penetrate the mitochondrial membrane unlike CRISPR-Cas, base editors, and prime editors. We expect to submit an IND and/or CTA for PBGENE-PMM in 2025 for this program.
  - **PBGENE-NVS** (Gene Insertion Program) – Our research team has made excellent progress advancing our gene insertion program with Novartis to develop a custom ARCUS nuclease for patients with sickle cell disease and beta thalassemia.
  - **iECURE-OTC** (Gene Insertion Program) - We are pleased with the progress being made by our partner iECURE to advance the first ARCUS-mediated gene editing program into clinical trials following approvals in the United States, United Kingdom, and Australia for initiation of the phase1/2 OTC-HOPE study. **ECURE-506 is the most advanced ARCUS *in vivo* gene editing program with first-in-human clinical dosing ready to commence in 2024.** The OTC-HOPE study is evaluating ECUR-506 as a potential treatment for neonatal onset ornithine transcarbamylase (OTC) deficiency. ECURE-506 provides important regulatory and clinical validation for ARCUS.
  - **Prevail Collaboration** – Most recently, we exercised the option to return three programs from Prevail Therapeutics following the decision to conclude the collaboration. **These programs, starting with the lead Duchenne Muscular Dystrophy program, are very important for people born with incurable genetic diseases and have the potential to substantially increase the valuation of Precision while also attracting**
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**new partners with key gene editing capabilities.** Through the collaboration we gained deeper insights into the applications where ARCUS is uniquely differentiated, advanced three programs from concept toward clinical candidates, and generated proof of concept data for ARCUS gene excision and gene insertion.

In closing, **our near-term fundamentals are strong, and the long-term is potentially even brighter with the opportunity to develop three newly returned advanced pre-clinical programs in large patient populations with high unmet need.**

- Our lead partnered program for **OTC deficiency is rapidly moving to the clinic in 2024.**
- Our first wholly owned program for **hepatitis B is on track for an expected filing in 2024.**
- Our second wholly owned program for **PMM is on track for an expected filing in 2025.**
- After monetizing our CAR T assets to raise approximately \$50 million in cash and potential near-term milestones, we completed a \$40 million public offering **extending our anticipated cash runway into the second half of 2026.**
- Our team is singularly focused on achieving clinical validation of ARCUS *in vivo* gene editing.

**Thank you to our loyal stockholders. Your support has been instrumental in our progress to date and has enabled us to build a stronger, more focused Precision BioSciences.**

Warm Regards,

Michael Amoroso

Chief Executive Officer

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**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, 2023

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**

(State or other jurisdiction of  
incorporation or organization)

**20-4206017**

(I.R.S. Employer  
Identification No.)

**302 East Pettigrew St., Suite A-100**

**Durham, North Carolina**  
(Address of principal executive offices)

**27701**

(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 Capital 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	<input type="checkbox"/>	Accelerated filer	<input type="checkbox"/>
Non-accelerated filer	<input checked="" type="checkbox"/>	Smaller reporting company	<input checked="" type="checkbox"/>
		Emerging growth company	<input checked="" type="checkbox"/>

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

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

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to §240.1D-1(b).

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

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the Registrant, based on the closing price of the shares of common stock on The Nasdaq Capital Market on June 30, 2023, was \$59.1 million.

The number of shares of registrant's common stock outstanding as of March 21, 2024 was 6,916,239.

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, 2023, 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

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## 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, planned preclinical studies and clinical trials, or discontinuance thereof, the status and results of our preclinical studies, expected release of interim data, 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, potential new application filings and regulatory approvals, research and development costs, timing, expected results and likelihood of success, as well as plans and objectives of management for future operations 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 to advance our programs;
- risks associated with raising additional capital and requirements under our current debt instruments and effects of restrictions thereunder;
- 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;
- 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' or other licensees' 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;
- delays or difficulties in our or 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 any pandemic, epidemic, or outbreak of an infectious disease;
- the success of our existing collaboration and other license 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; and
- our ability to meet the requirements of and maintain listing of our common stock on Nasdaq or other public stock exchanges.

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.

## 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.*
- *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 or other licensees 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.*
- *Our failure to meet the continued listing requirements of The Nasdaq Capital Market could result in a delisting of our common stock.*

## PART I

### Item 1. Business.

We are an advanced gene editing company utilizing our novel proprietary ARCUS platform to develop *in vivo* gene editing therapies for sophisticated gene edits, including gene elimination, insertion, and excision. ARCUS is the only gene editor derived purely from a protein, called a homing endonuclease, that evolved in nature to safely edit a genome and add function. ARCUS is particularly efficient at generating defined outcomes due to predominant repair using homology directed repair (“HDR”) as opposed to non-homologous end joining (“NHEJ”).

#### 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.

There are several genome editing technologies, including ARCUS, zinc-finger nucleases (“ZFNs”), TAL-effector nucleases (“TALENs”), CRISPR-Cas, 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. In addition to the importance of efficiency, or the percentage of cells that are edited on-target, we believe ARCUS is differentiated by the type of edit predictably driving a more defined outcome. A defined outcome is a predictable, highly consistent, and intended therapeutic edit, as compared to a random outcome, a distribution of inconsistent edits which could potentially limit efficacy and the safety profile.

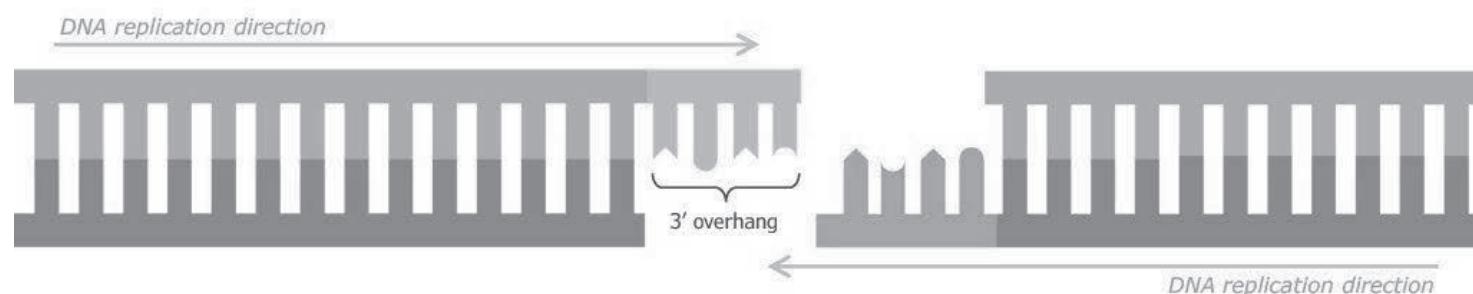
## Our ARCUS Genome Editing Platform

ARCUS has three unique properties that can lead to defined outcomes:

**The Cut.** ARCUS has a unique cut that was evolved to drive defined outcomes. As shown in Figure 1 below, ARCUS generates a staggered cut that produces a 4 base pair, single strand of DNA. The portions noted in pink and blue are critical to finding a matching sequence on a DNA template when inserting a gene. These overhangs are also in the same direction as DNA replication, so once it finds the matching sequence, it can start DNA replication on the template and incorporate the intended edit into the genome. This process is known as HDR.

ARCUS also evolved for the pink and blue portions to match each other similar to puzzle pieces. If a DNA template is not inserted, no scar is made at the cut site. We can take advantage of this perfect re-ligation, or re-matching of the pieces, by making two cuts in the DNA strand so the overhangs match in an excision, a type of sophisticated edit.

Figure 1.



**The Size.** Size affects the ease and versatility with which endonucleases can be delivered to cells for editing. ARCUS can use different delivery vehicles including lipid nanoparticles (“LNP”) for the liver and adeno-associated viruses (“AAV”) to target diverse tissue types as it is very small relative to other genome editing endonucleases. ARCUS is also uniquely able to include an insertion DNA template in the same AAV because of its small size, which allows targeting *in vivo* gene insertion at tissues beyond the liver. ARCUS has demonstrated editing in a breadth of diverse tissue types, including the liver, muscle, the central nervous system, hematopoietic stem cells, and the eye.

**The simplicity.** ARCUS is the only single component editor. As a single protein with a DNA recognition motif and catalytic activity all in one, no guide RNA is required. Because editing outcomes are not dependent on simultaneous delivery of multiple editor components in separate delivery vehicles, ARCUS may lead to higher efficiency with potentially lower AAV and LNP doses.

## 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 genetic and infectious diseases. In 2023 and early 2024, we refocused our pipeline on our core foundational strength as an *in vivo* gene editing company with the strategic divestment of our lead *ex vivo* allogeneic chimeric antigen receptor (“CAR”) T candidate, azercabtagene zapreleucel (“azer-cel”). In 2024, our strategy is solely focused on progressing our gene editing portfolio, including programs under development internally and with partners, and differentiating ARCUS as a unique tool in the gene editing field.

## *In vivo* Gene Editing Pipeline

### Wholly-Owned Programs

**PBGENE-HBV (Elimination).** We expect to submit an investigational new drug application (“IND”) and/or clinical trial application (“CTA”) in 2024 for our PBGENE-HBV program for the potential treatment of chronic hepatitis B virus (“HBV”). HBV causes inflammation and damage to the liver, leading to chronic infection and increased risk of death from liver cancer or cirrhosis. There is no cure for chronic hepatitis B, and current treatments rarely result in functional cure, primarily due to persistence of viral DNA in the liver. In patients with chronic HBV, genetic material of the virus is converted within infected liver cells into covalently closed circular DNA (“cccDNA”) that acts as a template to make HBV copies. HBV also inserts its DNA into the human genome of infected liver cells. This integrated HBV DNA produces the viral protein, hepatitis B surface antigen (“HBsAg”), which is secreted in the blood. Presence of HBsAg is associated with poorer outcomes and elimination of HBsAg is necessary for functional cure of chronic HBV.



PBGENE-HBV is designed to eliminate cccDNA with direct cuts and edits as well as to inactivate integrated HBV DNA with the goal of long-lasting reductions in HBsAg. We believe specificity is of particular importance for developing a safe gene editing approach to eliminating HBV, as a lack of nuclease specificity can lead to unfavorable off-target results including increased integrations of HBV genomes into the human genome, as well as translocations between integrations. Preclinical data from the PBGENE-HBV program presented at scientific congresses in 2023 highlighted that ARCUS nucleases exhibited high levels of on-target editing and demonstrated substantial reductions of both intracellular cccDNA and secreted HBsAg with no detectable translocations in primary human hepatocytes.

**PBGENE-PMM (Elimination).** We are pursuing development of PBGENE-PMM as a potential first-in-class opportunity for treatment of m.3243 associated primary mitochondrial myopathy (“PMM”). Mitochondrial diseases are the most common hereditary metabolic disorder, affecting 1 in 4,300 people. PMM currently lacks a curative treatment and impacts approximately 50% of patients with mitochondrial disease. The high specificity and single component nature of our mitoARCUS nucleases are designed to enable specific editing of mutant mitochondrial DNA while allowing normal (wild-type) mitochondrial DNA to repopulate in the mitochondria and restore normal function. We expect to submit an IND and/or CTA in 2025.

## Partnered Programs

**PBGENE-NVS (Insertion).** In connection with our exclusive *in vivo* gene editing research and development collaboration and license agreement (the “Novartis Agreement”) with Novartis Pharma AG (“Novartis”), 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.

**PBGENE-DMD (Excision), PBGENE-LL2 (Insertion) and PBGENE-LL3.** We continue our *in vivo* gene editing collaboration with Prevail Therapeutics, Inc. (“Prevail”), a wholly-owned subsidiary of Eli Lilly and Company (“Lilly”), in applying ARCUS nucleases to three initial targets, including Duchenne muscular dystrophy (“DMD”) in muscle, a liver directed target (PBGENE-LL2) and a central nervous system directed target (PBGENE-LL3). 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 complementary ARCUS nucleases delivered by a single AAV to excise 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. During our September 2023 Research and Development (“R&D”) Day, we highlighted preclinical data demonstrating the potential of ARCUS *in vivo* gene editing for large gene excisions and that the edited dystrophin variant was observed in multiple tissue types frequently involved in progression of DMD, including skeletal muscle, heart, and diaphragm, thereby enabling significantly improved muscle function. Also during our R&D Day, we highlighted new data demonstrating that ARCUS is capable of high efficiency gene insertion in nondividing cells in adult nonhuman primates, the most challenging context for gene insertion. In the pre-clinical study involving coadministration of AAV and lipid nanoparticle, our scientists observed 40% to 45% overall gene insertion efficiency at 1- and 3-months. Our scientists largely attribute this high efficiency to the unique ARCUS cut type which drives homology directed repair, even in nondividing cells.

**iECURE-OTC (Insertion).** In partnership with iECURE, Inc. (“iECURE”), an ARCUS-mediated gene insertion approach is being pursued as a potential treatment option for neonatal onset ornithine transcarbamylase (“OTC”) deficiency. Non-human primate (“NHP”) 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 NHPs with high efficiency. iECURE received approval from the Australian Therapeutic Goods Administration for the initiation of a first-in-human Phase 1/2 trial evaluating ECUR-506, incorporating an ARCUS nuclease for the treatment of OTC deficiency in pediatric (or neonatal) patients. In March 2024, iECURE also received approval from the U.K. Medicines & Healthcare products Regulatory Agency for the company’s CTA application to expand the Phase 1/2 OTC-HOPE study evaluating ECUR-506 into the U.K. iECURE is preparing sites and anticipates initiating the global clinical trial in the first half of 2024.

## 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 gene therapies, including our co-founder, who has been working with genome editing technology for over 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 gene therapies. As of December 31, 2023, our team of Precisioneers included 29 full-time employees with Ph.D. or M.D. degrees.

## License and Collaboration Agreements

### *Caribou Biosciences*

In February 2024, we announced that we had granted Caribou Biosciences, Inc., (“Caribou”) a leading CRISPR genome-editing cell therapy company, a non-exclusive, worldwide license, with the right to sublicense, to one of our foundational cell therapy patent families for use with CRISPR-based therapies in the field of human therapeutics. Under the terms of the agreement, we received an upfront payment and, upon commercialization by Caribou, will receive royalties on net sales of licensed products.

### *TG Therapeutics*

On January 7, 2024, we entered into a license agreement (the “TG License Agreement”) with TG Cell Therapy, Inc. (“TG Subsidiary”) and its parent company TG Therapeutics, Inc. (“TG Parent” and, together with TG Subsidiary, “TG Therapeutics”), pursuant to which we granted TG Subsidiary certain exclusive and non-exclusive license rights to develop, manufacture, and commercialize azer-cel for autoimmune diseases and other indications outside of cancer. Refer to Part II. Item 7. “Management’s Discussion and Analysis of Financial Condition and Results of Operations” of this Annual Report on Form 10-K for additional information related to the terms, duration, and effect of the TG License Agreement.

### *Sale of CAR T Platform to Imugene*

On August 15, 2023 we entered into an asset purchase agreement (the “Imugene Purchase Agreement”) with Imugene Limited, and its wholly-owned subsidiary Imugene (USA) Inc. (“Imugene US” and, together with Imugene Limited, “Imugene”). Pursuant to and simultaneously with the execution of the Imugene Purchase Agreement, on August 15, 2023 (the “Closing Date”), Imugene US acquired our manufacturing infrastructure used in the development and manufacture of azer-cel, including assuming the lease to our manufacturing facility and certain contracts with respect to our manufacturing facility, and related equipment, supplies, azer-cel clinical trial inventory and other assets related to our CAR T cell therapy platform. As part of the Imugene Purchase Agreement, Imugene US hired a number of our employees who were associated with our historical CAR T cell therapy operations.

Additionally, we entered into a license agreement with Imugene (the “Imugene License Agreement”) on the Closing Date, pursuant to which we granted Imugene US certain exclusive and non-exclusive license rights to develop, manufacture, and commercialize oncological applications of our allogeneic CAR T therapy, azer-cel, and up to three additional research product candidates directed to targets that Imugene US may nominate prior to the fifth anniversary of the effective date of the Imugene License Agreement, pursuant to the terms of the Imugene License Agreement. Refer to Part II. Item 7. “Management’s Discussion and Analysis of Financial Condition and Results of Operations” of this Annual Report on Form 10-K for additional information related to the terms, duration, and effect of the Imugene License Agreement.

### *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 collectively referred to as licensed products). Any initial licensed products under the Novartis Agreement 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. Refer to Part II. Item 7. “Management’s Discussion and Analysis of Financial Condition and Results of Operations” of this Annual Report on Form 10-K for additional information related to the terms, duration, and effect of the Novartis Agreement.



### *Prevail Therapeutics, Inc.*

On November 19, 2020, we entered into a development and license agreement with Lilly to collaborate to discover and develop *in vivo* gene editing products incorporating our ARCUS nucleases to utilize ARCUS for the research and development of potential *in vivo* therapies for genetic disorders (the “Original Prevail Agreement”). This agreement was subsequently assigned to Prevail, effective November 1, 2022.

On June 30, 2023, we entered into a license agreement (the “Prevail Agreement”) with Prevail, which amended and restated the Original Prevail Agreement. Pursuant to the terms of the Prevail Agreement, we and Prevail will continue to collaborate on developing our ARCUS nucleases for the research and development of potential *in vivo* therapies for genetic disorders, including DMD, a liver-directed target, and a central nervous system directed target. Prevail also continues to have the right to nominate up to three additional gene targets for genetic disorders over the initial nomination period of four years. Prevail may extend the nomination period for an additional two years from the date on which such initial nomination period ends, upon Prevail’s election and payment of an extension fee. Additionally, Prevail has the option to replace up to two gene targets upon Prevail's election and payment of a replacement target fee.

Prevail will oversee and fund preclinical research and IND-enabling activities following creation, selection, *in vitro* development, and optimization of ARCUS nucleases with respect to the gene targets subject to the collaboration, which were previously conducted by us at our expense. Manufacturing initial clinical trial material for the first licensed product, which was previously our responsibility to conduct at Prevail’s expense, will instead be Prevail’s responsibility at Prevail’s expense. Prevail will continue to 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. Refer to Part II. Item 7. “Management’s Discussion and Analysis of Financial Condition and Results of Operations” of this Annual Report on Form 10-K for additional information related to the terms, duration, and effect of the Prevail Agreement.

### *iECURE*

In August 2021, we entered into a development and license agreement with iECURE (the “iECURE DLA”) under which iECURE was to advance our PBGENE-PCSK9 candidate for familial hypercholesterolemia (“FH”) through preclinical activities as well as a Phase 1 clinical trial in order to gain access to 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, Phenylketonuria, and another program focused on liver disease (the “PCSK9 License”). In 2022 we 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 DLA, we entered into an Equity Issuance Agreement with iECURE (the “iECURE Equity Agreement”), pursuant to which iECURE issued us common stock in iECURE as additional consideration for the license to use our PCSK9-directed ARCUS nuclease.

In December 2023, iECURE announced that the Australian Therapeutic Goods Administration had approved its Clinical Trial Notification for ECUR-506, an investigational therapy incorporating an ARCUS nuclease in development for the treatment of OTC deficiency in pediatric (or neonatal) patients. In March 2024, iECURE announced that the U.K. Medicines & Healthcare products Regulatory Agency had approved its Clinical Trial Authorisation application to expand the OTC-HOPE study into the U.K. iECURE plans to initiate its global first-in-human Phase 1/2 clinical study of ECUR-506 in the first half of 2024.

### *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.

#### *Collectis S.A.*

In January 2014, we entered into a cross-license agreement with Collectis S.A., which we refer to as the Collectis License, in connection with a settlement of litigation matters (1) between Collectis and us and (2) among Collectis, Duke and us. Collectis granted us a non-exclusive, sublicensable, worldwide, fully paid, royalty-free license to certain modified I-CreI homing endonuclease patents and Collectis 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 Collectis is subject to the rights of a preexisting license agreement that Collectis entered into with a third party, and the license granted to us excludes any rights exclusively granted by Collectis 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 Collectis 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 Collectis and us and (2) among Collectis, 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 Collectis due to the preexisting license.

The Collectis 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 Collectis 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 and epigenomic editing technology in the human health sector, including companies such as Beam Therapeutics, Inc., CRISPR Therapeutics, AG, Editas Medicine, Inc., Intellia Therapeutics, Inc., Prime Medicine, Inc., Tune Therapeutics, 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 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 *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, 2023, 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, 2023, we own 42 issued U.S. patents, 46 pending non-provisional U.S. patent applications, and 10 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 patents in the United States, nine issued patents in Europe, three issued patents in Japan, 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 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 patents in the United States, 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 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, Mexico, and South Korea. 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.

### ***In Vivo Gene Editing Patent Families***

We own 28 patent families, including three jointly-owned patent families, that are directed to our *in vivo* gene editing technologies. Each of our *in vivo* gene editing product candidates is protected or disclosed by one or more of these patent families.

The first family includes three issued patents in the United States, two issued patents in Japan, one issued patent in each of Europe, Eurasia, South Korea, and Hong Kong, and pending patent applications in each of the United States, Europe, Australia, Canada, China, Eurasia, Guatemala, Hong Kong, Israel, Japan, South Korea, Mexico, Morocco, the Philippines, Saudi Arabia, and Thailand. Patents in this family include claims directed to (1) first-generation engineered meganucleases that cleave a recognition sequence within the genome of the Hepatitis B virus, (2) nucleic acids encoding such engineered meganucleases, (3) viral vectors comprising nucleic acids encoding such engineered meganucleases, (4) lipid nanoparticle compositions comprising nucleic acids encoding such engineered meganucleases, (5) pharmaceutical compositions comprising such engineered meganucleases, nucleic acids, viral vectors, and lipid nanoparticle compositions, and (6) methods for treating patients having HBV by administration of such engineered meganucleases or nucleic acids encoding such engineered meganucleases. Patents in this family have a standard expiration date of October 13, 2037, subject to potential extensions.

The second family includes two issued patents in the United States, and pending patent applications in each of the United States and Europe. Patents in this family include claims directed to (1) second-generation engineered meganucleases that cleave a recognition sequence within the genome of the Hepatitis B virus, (2) nucleic acids encoding such engineered meganucleases, (3) viral vectors comprising nucleic acids encoding such engineered meganucleases, (4) lipid nanoparticle compositions comprising nucleic acids encoding such engineered meganucleases, (5) pharmaceutical compositions comprising such engineered meganucleases, nucleic acids, viral vectors, and lipid nanoparticle compositions and, (6) methods for treating patients having HBV by administration of such engineered meganucleases or nucleic acids encoding such engineered meganucleases. 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, Hong Kong, and New Zealand. Patents in this family include claims directed to (1) third-generation engineered meganucleases that cleave a recognition sequence within the genome of the Hepatitis B virus, (2) nucleic acids encoding such engineered meganucleases, (3) recombinant viruses comprising nucleic acids encoding such engineered meganucleases, (4) lipid nanoparticle compositions comprising nucleic acids encoding such engineered meganucleases, (5) pharmaceutical compositions comprising such engineered meganucleases, nucleic acids, recombinant viruses, and lipid nanoparticle compositions and, (6) methods for treating patients having HBV by administration of such engineered meganucleases or nucleic acids encoding such engineered meganucleases. Patents in this family, if issued, will have a standard expiration date of December 4, 2040, subject to potential extensions.

The fourth family, which we jointly own, includes a pending PCT international patent application, and pending patent applications in each of the United States, Europe, Australia, Canada, and Japan. Patents in this family include claims directed to (1) mitochondrial-targeting engineered meganucleases (MTEM)s that cleave recognition sequences within the mitochondrial genome of a eukaryotic cell, (2) nucleic acids encoding such MTEMs, (3) recombinant viruses comprising nucleic acids encoding such MTEMs, (4) lipid nanoparticle compositions comprising nucleic acids encoding such MTEMs, (5) pharmaceutical compositions comprising such MTEMs, nucleic acids, recombinant viruses, and lipid nanoparticle compositions, (6) genetically modified eukaryotic cells comprising nucleic acids encoding such MTEMs, (7) methods of producing genetically modified eukaryotic cells and populations of genetically modified eukaryotic cells by delivering such MTEMs, (8) methods for degrading mutant mitochondrial genomes in target cells or populations of target cells by delivery of such recombinant meganucleases, and (9) methods for treating conditions associated with mitochondrial disorders by administration of such MTEMs. Patents in this family, if issued, will have a standard expiration date of April 22, 2042.

The fifth family, which we jointly own, includes a pending PCT international patent application, two pending patent applications in the United States, and pending patent applications in each of Europe, Australia, Canada, China, Israel, Japan, Mexico, and South



Korea. Patents in this family include claims directed to (1) mitochondrial-targeting engineered meganucleases (MTEM)s that cleave a recognition sequence within the mitochondrial genome of a eukaryotic cell, (2) nucleic acids encoding such MTEMs, (3) recombinant viruses comprising nucleic acids encoding such MTEMs, (4) lipid nanoparticle compositions comprising nucleic acids encoding such MTEMs, (5) pharmaceutical compositions comprising such MTEMs, nucleic acids, recombinant viruses, and lipid nanoparticle compositions, (6) genetically modified eukaryotic cells comprising nucleic acids encoding such MTEMs, (7) methods of producing genetically modified eukaryotic cells and populations of genetically modified eukaryotic cells with such MTEMs, (8) methods for degrading mutant mitochondrial genomes in target cells or populations of target cells by delivery of such recombinant meganucleases, and (9) methods for treating conditions associated with mitochondrial disorders by administration of such MTEMs. Patents in this family, if issued, will have a standard expiration date of April 22, 2042, subject to potential extensions.

The sixth family includes one issued patent in each of Europe and Japan, and pending patent applications in each of the United States, Europe, Australia, Canada, Hong Kong, and Japan. Patents in this family include claims directed to (1) methods for treating DMD by utilizing pairs of engineered nucleases to remove an exon from the dystrophin gene and (2) methods for removing DNA sequences from the genome of a cell by utilizing pairs of engineered nucleases. Patents in this family will have a standard expiration date of March 12, 2035, subject to potential extensions.

The seventh family includes one issued patent in the United States, two pending patent applications in the United States, and pending patent applications in each of Europe, Australia, Canada, China, Israel, Japan, Mexico, and South Korea. Patents in this family include claims directed to (1) engineered meganucleases that cleave recognition sequences within the dystrophin gene, (2) nucleic acids encoding such engineered meganucleases, (3) recombinant viruses comprising nucleic acids encoding such engineered meganucleases, (4) lipid nanoparticle compositions comprising nucleic acids encoding such engineered meganucleases, (5) pharmaceutical compositions comprising such engineered meganucleases, nucleic acids, recombinant viruses, and lipid nanoparticle compositions, (6) methods of producing genetically modified eukaryotic cells having a modified dystrophin gene with such engineered meganucleases, (7) methods of modifying a dystrophin gene in a subject by delivering such engineered meganucleases to a target cell, and (8) methods for treating DMD, which is characterized by a mutation within the dystrophin gene, by administering such engineered meganucleases. Patents in this family will have a standard expiration date of November 12, 2041.

The eighth family includes one issued patent in each of the United States, Europe, Australia, China, Israel, Japan, Mexico, and South Korea, two pending patent applications in each of the United States and Japan, and pending patent applications in each of Europe, Australia, Canada, China, Hong Kong, Israel, Mexico, and South Korea. Patents in this family include claims directed to (1) engineered meganucleases that cleave recognition sequences within a PCSK9 gene, (2) nucleic acids encoding such engineered meganucleases, (3) recombinant viral vectors comprising nucleic acids encoding such engineered meganucleases, (4) pharmaceutical compositions comprising such engineered meganucleases, nucleic acids, and recombinant viral vectors, and (5) methods for reducing expression of PCSK9 in a subject by administering such engineered meganucleases. Patents in this family will have a standard expiration date of April 20, 2038, subject to potential extensions.

The ninth family includes a pending PCT international patent application. Patents in this family include claims directed to (1) polynucleotides comprising template nucleic acids for insertion in a SERPINA1 gene, (2) recombinant viruses comprising such polynucleotides, (3) lipid nanoparticle compositions comprising such polynucleotides, (4) pharmaceutical compositions comprising such polynucleotides, (5) methods of producing genetically modified eukaryotic cells having a modified SERPINA1 gene by introduction of such engineered meganucleases and such template nucleic acids to a eukaryotic cell, (6) methods of modifying a SERPINA1 gene in a target cell by introduction of such engineered meganucleases and such template nucleic acids to a target cell, and (7) methods of treating AAT deficiency in a subject by administering pharmaceutical compositions comprising such engineered meganucleases and such template nucleic acids to a subject. Patents in this family, if issued, will have a standard expiration date of October 19, 2042.

The tenth family includes a pending PCT international patent application. Patents in this family include claims directed to (1) second generation engineered meganucleases that cleave recognition sequences within a SERPINA1 gene, (2) nucleic acids encoding such engineered meganucleases, (3) recombinant viruses comprising nucleic acids encoding such engineered meganucleases, (4) lipid nanoparticle compositions comprising nucleic acids encoding such engineered meganucleases, (5) pharmaceutical compositions comprising such engineered meganucleases, nucleic acids, recombinant viruses, and lipid nanoparticle compositions, (6) polynucleotides comprising template nucleic acids for insertion in a SERPINA1 gene, (7) recombinant viruses comprising such template nucleic acids, (8) lipid nanoparticle compositions comprising such template nucleic acids, (9) pharmaceutical compositions comprising such template nucleic acids, (10) methods of producing genetically modified eukaryotic cells having a modified SERPINA1 gene by introduction of such engineered meganucleases and such template nucleic acids to a eukaryotic cell, (11) methods of modifying a SERPINA1 gene in a target cell by introduction of such engineered meganucleases and such template nucleic acids to a target cell, and (12) methods of treating AAT deficiency in a subject by administering pharmaceutical compositions comprising such engineered meganucleases and such template nucleic acids to a subject. Patents in this family, if issued, will have a standard expiration date of October 19, 2042.

The eleventh family includes two issued patents in each of the United States and Japan, one issued patent in Australia, pending patent applications in each of the United States, Europe, Australia, and Canada, and two pending patent applications in Japan. Patents in this family include claims directed to (1) first generation engineered meganucleases that cleave recognition sequences within a mutant rhodopsin gene, (2) nucleic acids encoding such engineered meganucleases, (3) recombinant AAV vectors comprising nucleic acids encoding such engineered meganucleases, and (4) methods for treating retinitis pigmentosa by administering such engineered meganucleases. Patents in this family will have a standard expiration date of September 8, 2036, subject to potential extensions.

The twelfth family includes pending patent applications in each of the United States, Europe, and Canada. Patents in this family include claims directed to (1) second generation engineered meganucleases that cleave recognition sequences within a mutant rhodopsin gene, (2) nucleic acids encoding such engineered meganucleases, (3) recombinant viruses comprising nucleic acids encoding such engineered meganucleases, (4) lipid nanoparticle compositions comprising nucleic acids encoding such engineered meganucleases, (5) genetically modified eukaryotic cells comprising nucleic acids encoding such engineered meganucleases, (7) genetically modified eukaryotic cells comprising a modified rhodopsin gene, (8) methods of producing genetically modified eukaryotic cells having a disrupted target sequence in a chromosome by introduction of such engineered meganucleases, (9) methods of producing genetically modified eukaryotic cells having an exogenous sequence of interest inserted in a chromosome by introduction of such engineered meganucleases and a nucleic acid having the sequence of interest, (10) pharmaceutical compositions comprising such engineered meganucleases, nucleic acids, recombinant viruses, and lipid nanoparticle compositions, and (11) methods for treating retinitis pigmentosa by administering such engineered meganucleases or such pharmaceutical compositions. Patents in this family, if issued, will have a standard expiration date of May 11, 2041, subject to potential extensions.

The thirteenth family includes pending patent applications in each of the United States and Europe. Patents in this family include claims directed to (1) engineered meganucleases that cleave recognition sequences within an HAO1 gene, (2) nucleic acids encoding such engineered meganucleases, (3) viral vectors comprising nucleic acids encoding such engineered meganucleases, (4) methods of producing genetically modified eukaryotic cells having a disrupted target sequence in a chromosome by introduction of such engineered meganucleases, (5) methods of producing genetically modified eukaryotic cells having an exogenous sequence of interest inserted in a chromosome by introduction of such engineered meganucleases and a nucleic acid having the sequence of interest, (6) methods of producing genetically modified eukaryotic cells having a modified HAO1 gene by introduction of such engineered meganucleases, (7) genetically modified eukaryotic cells made by such methods, (8) genetically modified eukaryotic cells comprising a modified HAO1 gene, (9) pharmaceutical compositions comprising such engineered meganucleases and nucleic acids encoding such engineered meganucleases, (10) methods for treating primary hyperoxaluria type I by administering such engineered meganucleases, and (11) recombinant HAO1 polypeptides lacking a functional peroxisomal targeting signal. Patents in this family, if issued, will have a standard expiration date of December 20, 2039, subject to potential extensions.

The fourteenth family includes pending patent applications in each of the United States, Europe, and Canada. Patents in this family include claims directed to (1) engineered meganucleases that cleave recognition sequences within an HAO1 gene, (2) nucleic acids encoding such engineered meganucleases, (3) recombinant viruses comprising nucleic acids encoding such engineered meganucleases, (4) lipid nanoparticle compositions comprising nucleic acids encoding such engineered meganucleases, (5) pharmaceutical compositions comprising such engineered meganucleases, nucleic acids, recombinant viruses, and lipid nanoparticle compositions, (6) methods of producing genetically modified eukaryotic cells having a modified HAO1 gene with such engineered meganucleases, (7) methods of modifying an HAO1 gene in a subject by delivering such engineered meganucleases to a target cell, (8) genetically modified eukaryotic cells made by such methods, (9) genetically modified eukaryotic cells comprising a modified HAO1 gene, and (10) methods for treating primary hyperoxaluria type I by administering such engineered meganucleases. Patents in this family, if issued, will have a standard expiration date of January 7, 2042, subject to potential extensions.

The fifteenth family includes one issued patent in each of the United States, Europe, and Australia, and pending patent applications in each of the United States, Europe, Australia, Canada, and Japan. Patents in this family include claims directed to (1) engineered meganucleases that cleave recognition sequences within the int22h-1 region of the Factor VIII gene, (2) nucleic acids encoding such engineered meganucleases, (3) viral vectors comprising nucleic acids encoding such engineered meganucleases, (4) pharmaceutical compositions comprising such engineered meganucleases or nucleic acids encoding such engineered meganucleases, and (5) methods for treating hemophilia A by administration of such pharmaceutical compositions. Patents in this family will have a standard expiration date of May 3, 2037, subject to potential extensions.

The sixteenth family includes pending patent applications in each of the United States and Europe. Patents in this family include claims directed to (1) engineered meganucleases that cleave recognition sequences within the int22h-1 region of the Factor VIII gene, (2) nucleic acids encoding such engineered meganucleases, (3) viral vectors comprising nucleic acids encoding such engineered meganucleases, (4) pharmaceutical compositions comprising such engineered meganucleases or nucleic acids encoding such engineered meganucleases, (5) methods for treating hemophilia A by administration of such pharmaceutical compositions, (6) methods for genetically modifying a Factor VIII gene in a mammalian cell by introducing such engineered meganucleases, and (7) genetically-modified cells made by such methods. Patents in this family, if issued, will have a standard expiration date of November 1, 2038, subject to potential extensions.

The seventeenth family includes pending patent applications in each of the United States, Europe, Australia, Canada, and Japan. Patents in this family include claims directed to (1) engineered meganucleases that cleave recognition sequences within a transthyretin (TTR) gene, (2) nucleic acids encoding such engineered meganucleases, (3) recombinant viruses comprising nucleic acids encoding such engineered meganucleases, (4) methods of producing genetically modified eukaryotic cells having a disrupted target sequence in a chromosome by introduction of such engineered meganucleases, (5) methods of producing genetically modified eukaryotic cells having an exogenous sequence of interest inserted in a chromosome by introduction of such engineered meganucleases and a nucleic acid having the sequence of interest, (6) methods of producing genetically modified eukaryotic cells having a modified TTR gene by introduction of engineered nucleases, (7) methods for modifying a TTR gene by delivering such engineered meganucleases, (8) genetically modified eukaryotic cells made by such methods, (9) genetically modified eukaryotic cells comprising a modified TTR gene, (10) lipid nanoparticle compositions comprising such engineered meganucleases, and (11) pharmaceutical compositions comprising such engineered meganucleases and lipid nanoparticle compositions. Patents in this family, if issued, will have a standard expiration date of August 20, 2041, subject to potential extensions.

The eighteenth family includes one issued patent in Europe, and pending patent applications in each of the United States and Europe. Patents in this family include claims directed to (1) methods for treating subjects having nucleotide repeat expansion disorders, (2) pharmaceutical compositions comprising nucleases for treatment of nucleotide repeat expansion disorders, (3) engineered meganucleases that cleave recognition sequences within a frataxin (FXN) gene, (4) nucleic acids encoding such engineered meganucleases, (5) recombinant viral vectors comprising nucleic acids encoding such engineered meganucleases, and (6) methods for promoting precise deletion of loci flanked by repeat sequences in populations of eukaryotic cells. Patents in this family will have a standard expiration date of May 2, 2036, subject to potential extensions.

The nineteenth family includes one pending PCT international patent application. Patents in this family include claims directed to (1) polynucleotides comprising nucleic acids encoding heterologous proteins for expression, (2) recombinant viruses comprising such polynucleotides, (3) lipid nanoparticle compositions comprising such polynucleotides, (4) pharmaceutical compositions comprising such polynucleotides, recombinant viruses, and lipid nanoparticle compositions, (5) eukaryotic cells comprising such polynucleotides, (6) methods for expressing heterologous proteins in eukaryotic cells by introduction of such polynucleotides, (7) methods for producing genetically-modified eukaryotic cells by introduction of such polynucleotides encoding an engineered nuclease, and (8) methods for treating a disease in a subject by administration of such polynucleotides encoding a therapeutic protein. Patents in this family, if issued, will have a standard expiration date of January 6, 2043.

The twentieth family includes pending patent applications in each of the United States and Europe. Patents in this family include claims directed to (1) engineered meganucleases that cleave recognition sequences within a transferrin gene, (2) nucleic acids encoding such engineered meganucleases, (3) viral vectors comprising nucleic acids encoding such engineered meganucleases, (4) template nucleic acids for insertion within a transferrin gene, (5) methods of producing genetically modified eukaryotic cells having an exogenous sequence of interest inserted in a chromosome by introduction of such engineered meganucleases and a nucleic acid having the sequence of interest, (6) methods of producing genetically modified eukaryotic cells having a modified transferrin gene by introduction of engineered nucleases, (7) methods of producing genetically modified eukaryotic cells having a modified transferrin gene by introduction of engineered nucleases and a template nucleic acid, (8) genetically modified eukaryotic cells made by such methods, (9) genetically modified eukaryotic cells comprising a modified transferrin gene, (10) pharmaceutical compositions comprising such engineered meganucleases and template nucleic acids, and (11) methods for treating a disease by administration of such pharmaceutical compositions. Patents in this family, if issued, will have a standard expiration date of January 10, 2040, subject to potential extensions.

We own eight additional patent families that include pending provisional patent applications in the United States that are directed to *in vivo* gene editing. We will determine in the future whether to pursue each of these applications.

### ***Immunotherapy Patent Families***

We own 23 patent families, including one jointly-owned patent family, 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 patents in the United States, three issued patents in Israel, two issued patents in Europe and Hong Kong, one issued patent in each of Australia, China, Japan, and Mexico, 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 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, Europe, and Australia, one issued patent in each of 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 one issued patent in each of the United States, Europe, Israel, Japan, Mexico, and South Korea, and 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, Europe, 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) 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 two issued patents in Japan, one issued patent in each of Europe and Australia, 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) recombinant meganucleases that recognize and cleave a recognition sequence within the human  $\beta 2m$  gene, (2) nucleic acids and vectors encoding such recombinant meganucleases, (3) methods for producing genetically modified eukaryotic cells, including CAR T cells, using such meganucleases, (4) populations of genetically modified eukaryotic cells in which 80% of the cells have reduced expression of an endogenous TCR and 80% of the cells have reduced expression of  $\beta 2m$ , (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 sixth 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, and Japan. Patent applications in this family include claims directed to (1) nucleic acids encoding an engineered antigen receptor (e.g., a CAR) and an inhibitory molecule (e.g., an RNA interfering with  $\beta 2m$  expression), (2) genetically modified eukaryotic cells comprising such nucleic acids, (3) methods for producing such genetically modified eukaryotic cells using such nucleic acids and an engineered nuclease that promotes insertion of such nucleic acids, (4) genetically modified eukaryotic cells expressing an engineered antigen receptor and having expression of  $\beta 2m$  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 seventh family includes one issued patent in the United States, 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) 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 eighth family includes one issued patent in Europe, and pending patent applications in each of 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 will have a standard expiration date of October 3, 2038, subject to potential extensions.

The ninth 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 tenth family includes five issued patents in the United States, two issued patents in Israel, one issued patent in each of Europe, China, and Japan, and 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) 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 eleventh family includes 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 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 twelfth 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 thirteenth family includes 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 fourteenth family includes 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 fifteenth family includes 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 sixteenth family includes pending patent applications in each of the United States and Europe. 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 seventeenth family includes a pending patent application in the United States. 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 eighteenth family includes pending patent applications in each of the United States and Europe. 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.

The nineteenth family includes a pending PCT international patent application. Patent applications in this family include claims directed to (1) a method for reducing the number of target cells in a subject, (2) a method for reducing host rejection of genetically-modified human immune cells in a subject, and (3) a method for reducing nucleoside analog-induced killing of genetically-modified human immune cells in a subject. Patents in this family, if issued, will have a standard expiration date of November 3, 2042, subject to potential extensions.

The twentieth family includes a pending PCT international patent application. Patent applications in this family include claims directed to 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 November 15, 2042, subject to potential extensions.

The twenty-first family includes a pending PCT international patent application. Patent applications in this family include claims directed to (1) a method for reducing the number of cancer cells in a subject, and (2) a method for treating cancer in a subject who has relapsed following an autologous cell therapy. Patents in this family, if issued, will have a standard expiration date of December 9, 2042, subject to potential extensions.

We own one additional patent family that includes a pending provisional patent application in the United States that is directed to ARCUS nucleases useful in cell immunotherapy, and 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 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 and/or reduce the persistence of the vector after gene delivery. The first family includes one issued patent in each of the United States and Europe and pending patent applications in each of the United States and Europe. Patents in this family will have a standard expiration date of June 20, 2036, subject to potential extensions. The second family includes a 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 jointly own one patent family directed to methods for generating male sterile plants. This 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 April 22, 2042.

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 is 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 four registered trademarks in the United States, including ARCUS, ARC NUCLEASE, PRECISION BIOSCIENCES (Stylized) and PRECISION BIOSCIENCES. We also own registered trademarks for both ARCUS and ARC NUCLEASE in Australia, China, and Europe, a registered trademark for ARCUS in Canada, and registered trademarks for PRECISION BIOSCIENCES (Stylized) in Australia, Europe, and United Kingdom. Additionally, we own a pending trademark application for PRECISION BIOSCIENCES (Stylized) in Canada.

### ***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.

#### *Collectis S.A.*

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

In some cases, the FDA may require, or companies may voluntarily pursue, additional clinical trials after a product is approved to gain more information about the product. These so-called Phase 4 studies may be made a condition to approval of the BLA.

Concurrent with clinical trials, companies may complete additional animal studies and develop additional information about the biological characteristics of the product candidate, and must finalize a process for manufacturing the product in commercial quantities in accordance with cGMP. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, must develop methods for testing the identity, strength, 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, including results from 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 may be extended for a three month period for FDA to review additional information deemed a “major amendment” to an application. 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 may 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 any 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. The FDA may also require one or more Phase 4 post-market studies and additional 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, 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. Fast track designation applies to the combination of the product candidate and the specific indication for which it is being studied. The sponsor of a fast track product candidate has opportunities for more frequent interactions with the applicable FDA review team during product development and, once a BLA is submitted, the FDA may consider sections of the application 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.

Additionally, depending on the design of the applicable clinical trials, product candidates studied for their safety and effectiveness in treating serious or life-threatening diseases or conditions may be eligible for 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 conduct 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, and may require that such confirmatory trials be underway prior to granting any accelerated approval. 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 may 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 regulatory exclusivity periods and patent terms. This six-month exclusivity, which runs from the end of all existing periods of regulatory exclusivity or patent terms, 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 Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use ("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 EU 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 EU 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, 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 has been able to rely on a decision taken by the European Commission on the approval of a new (centralized procedure) MA when determining an application for a Great Britain MA (the European Commission Decision Reliance Procedure (“ECDRP”)); or use the MHRA’s mutual recognition or decentralized procedures (“MRDCRP”) which enabled MAs approved in EU member states (or Iceland, Liechtenstein, Norway) to be granted in GB. Since January 1, 2024, the new International Recognition procedure (“IRP”) has replaced the ECDRP which allows the MHRA to conduct targeted assessments by recognizing approvals from trusted partner agencies such as the European Commission. The MRDCRP is also incorporated under the umbrella of the IRP. Additionally, the ‘Unfettered Access Procedure’ enables an MA holder in Northern Ireland to seek recognition in GB.

There is 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, which aimed 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 MHRA published its consultation outcome on March 21, 2023 in which it confirmed that it would update the existing legislation. The resulting legislative changes, which are yet to be published, will ultimately determine the extent to which the UK regulations align with the (EU) CTR. Under the terms of the Protocol on Ireland and Northern Ireland, provisions of the (EU) CTR which relate to the manufacture and import of investigational medicinal products and auxiliary medicinal products currently apply in Northern Ireland.

## ***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.

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, which went into effect on April 1, 2013 and, due to subsequent legislative amendments to the statute will remain in effect through 2032, with the exception of a temporary suspension from May 1, 2020 through March 31, 2022, unless additional Congressional action is taken. On January 2, 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, reduced Medicare payments to several providers, including hospitals, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

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. On August 16, 2022, the Inflation Reduction Act of 2022, or IRA, was signed into law, which among other things, 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 Department of Health and Human Services (“HHS”) to implement many of these provisions through guidance, as opposed to regulation, for the initial years. On August 29, 2023, HHS announced the list of the first ten drugs that will be subject to price negotiations. HHS has issued and will continue to issue guidance implementing the IRA, although the Medicare drug price negotiation program is currently subject to legal challenges. While the impact of the IRA on the pharmaceutical industry cannot yet be fully determined, it is likely to be significant.

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.

In the EU, on December 13, 2021, Regulation No. 2021/2282 (the “Regulation”) 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 applicable, it will have a phased implementation depending on the concerned products. The Regulation intends to boost cooperation among EU member states in assessing health technologies, including new medicinal products, and provide the basis for cooperation at the EU level for joint clinical assessments in these areas. It 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 highest 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 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.

Dedicated to improving life 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 initiatives, 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. Through guest lectures, trainings, educational events, community outreach, 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 January 30, 2024, our workforce was self-reportedly approximately 50% female and approximately 24% Asian, Black, Latinx, two or more races, or not defined. Our senior leadership team and department heads were self-reportedly approximately 33% female and 24% Asian or Black as of January 30, 2024.

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, 2023, we had 109 full-time Precisioneers. Of these full-time employees, 78 are engaged in research and development activities and 29 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](http://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](http://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](http://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](http://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](http://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 \$61.3 million for the year ended December 31, 2023. As of December 31, 2023, we had an accumulated deficit of \$489.6 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 (“ATM”) 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;
- initiate potential 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;
- 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, license, 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 potential 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 potential 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 obtain sufficient funding on a timely basis or on favorable terms, we may be required to significantly delay, alter, reduce, or eliminate one or more of our research or product development programs and/or commercialization efforts, or to grant rights to develop and market products or product candidates that we would otherwise prefer to develop and market ourselves. We may also be otherwise unable to execute our business plan or growth strategy, or capitalize on business opportunities as desired. Any of these events could materially adversely affect our financial condition and business prospects.

We believe that, as of the date of this Annual Report on Form 10-K, existing cash and cash equivalents, expected operational receipts, including upfront and potential near-term consideration to be received from TG Therapeutics and other licensees, operational efficiencies gained from divestment of our historical CAR T operations, and availability of our ATM facility will be sufficient to fund our operating expenses and capital expenditure requirements into the second half of 2026. We expect our cash runway to be sufficient to achieve first-in-human Phase 1 clinical data for PBGENE-HBV and PBGENE-PMM. 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 and licensing arrangements.

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 potential 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 and other out-licensing relationships;
- the extent to which we exercise any development or commercialization rights under collaborative relationships;
- our ability to establish and maintain additional collaborative or other out-licensing 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. In addition, SEC regulations limit the amount that companies with a public float of less than \$75 million may raise during any 12-month period pursuant to a shelf registration statement on Form S-3.

***Provisions of our debt instruments may restrict our ability to pursue our business strategies, and our ability to access credit on favorable terms, if necessary, for the funding of our operations, trials and programs may be limited due to changes in credit markets.***

In May 2019, we 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 amount of \$30.0 million and the maturity date of the Revolving Line is June 23, 2024. As of December 31, 2023, 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.

Additionally, the credit markets and the financial services industry have been experiencing disruption characterized by the bankruptcy, failure, collapse or sale of various financial institutions, increased volatility in securities prices, diminished liquidity and credit availability and intervention from the U.S. and other governments. As a result, the cost and availability of credit has been and may continue to be adversely affected. We cannot be certain that funding under our Revolving Line will be available from PWB and the credit markets generally when and as needed, and if available, on acceptable terms if at all. If we are unable to obtain funding when needed and on acceptable terms, our financial condition and business prospects could be adversely impacted.

***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 ATM 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 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 familial hypercholesterolemia with iECURE as our partner in December 2022. 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.***

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. Due to the strategic transaction with Imugene for our azer-cel for cancer, as well as our CAR T infrastructure and cell therapy teams, and the TG License Agreement, we are now solely focused on leveraging our ARCUS genome editing platform to advance a new potential class of gene editing programs that go beyond gene knockouts in the liver and carry out sophisticated edits such as gene insertions, gene excision, and gene elimination in human therapeutics. 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. All of our *in vivo* 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 current and future product candidates 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, 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. Several companies have obtained FDA approval for autologous immunotherapies, and a number of companies 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 or other licensees to commercialize any products that we, our collaborators, or our other licensees 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, purity, and potency 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. For example, on November 28, 2023, the FDA announced that it was investigating reports of T-cell malignancies, including CAR-positive lymphoma, in patients who received treatment with BCMA- or CD19-directed autologous CAR T cell immunotherapies, and in January 2024, the FDA required the manufacturers of certain CAR-T therapies to add boxed warnings to product labeling cautioning against the risk of T-cell malignancies. Although we are no longer pursuing the development of CAR-T candidates following our strategic divestment of azer-cel, issues associated with these novel treatment modalities could lead to adverse public perceptions or otherwise affect the manner in which the FDA regulates gene editing products, such as those we are seeking to develop. 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 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 product candidates in the future, and we expect to file IND amendments to enable us to conduct 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 of such clinical trials. The manufacturing of *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 do not know whether any of our

planned or future 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 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. 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. 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”). 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.

***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 may 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. Our *in vivo* gene editing technology and 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. 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.

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 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 United 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 may seek orphan drug designation for our 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 or licensees obtain orphan drug designation for a product candidate, we or they 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 or licensees 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 or licensees 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 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.

If we or our collaborators or licensees 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.

***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.

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 eliminated the statutory Medicaid drug rebate cap beginning January 1, 2024. The rebate was previously capped at 100% of a drug's average manufacturer price.

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. On August 29, 2023, HHS announced the list of the first ten drugs that will be subject to price negotiations. HHS has issued and will continue to issue guidance implementing the IRA, although the Medicare drug price negotiation program is currently subject to legal challenges. 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 applicable, it will have a phased implementation depending on the concerned products. The Regulation intends to boost cooperation among EU member states in assessing health technologies, including new medicinal products, and provide the basis for cooperation at the EU level for joint clinical assessments in these areas. It 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 highest 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.

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 MHRA published its consultation outcome on March 21, 2023 in which it confirmed that it would update the existing legislation. The resulting legislative changes, which are yet to be published, will ultimately determine the extent to which the UK regulations align with the (EU) CTR. Under the terms of the Protocol on Ireland/Northern Ireland, provisions of the CTR which relate to the manufacture and import of investigational medicinal products 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, any resurgence of the virus or emergence of new variants may lead to further inspectional or administrative delays. If a prolonged government shutdown occurs, or if global health concerns 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 the needs of our business, which could disrupt our operations.***

As of December 31, 2023, we had 109 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 the then applicable needs of our business. 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.

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 our personnel needs. Due to our limited financial resources and the limited experience of our management team in managing a company with anticipated growth, we may not be able to effectively manage the expected demands of our operations or recruit and train additional qualified personnel. Moreover, addressing our personnel needs 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 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 and then applicable needs.

#### ***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 that involve the acquisition of or investment in 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, investments 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, investment 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. In addition, we are exposed to risks related to our investments, and we may realize losses in the fair value of our investments or a complete loss of our investments, which would have a negative effect on our financial condition. 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, investments 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 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 and/or a smaller reporting company with less than \$100 million in annual revenue in our last fiscal year, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. 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. 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 work 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. There can be no assurance that our cybersecurity risk management program and processes, including our policies, controls or procedures, will be fully implemented, complied with or effective in protecting our systems and information.

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 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, 2023, we had U.S. federal and state net operating loss ("NOL") carryforwards of \$195.0 million and \$166.8 million, respectively. Our federal NOL carryforwards carry forward indefinitely. Our state NOL carryforwards begin to expire in 2027. In addition, as of December 31, 2023, we have U.S. federal and state R&D tax credits of \$17.2 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 2029 and 2030, respectively. As of December 31, 2023, we had federal Orphan Drug credits of \$13.5 million, 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 (the "Code"). 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, 2023, we have a valuation allowance for the full amount of our net deferred tax assets as the realization of the net deferred tax assets is not determined to be more likely than not. In addition, Sections 382 and 383 of the Code limit a corporation's ability to utilize its 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.



## 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 Prevail 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 potential collaborators for other product research and development arrangements likely include large and mid-size pharmaceutical and biotechnology companies, and our potential collaborators for other technology research and development arrangements likely 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 continuing 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 Prevail 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.***

We 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 anticipate making 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 (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 (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. 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 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 30<sup>th</sup>. 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.

Additionally, we are a “smaller reporting company” as defined in Regulation S-K. Even after we no longer qualify as an emerging growth company, we may still qualify as a “smaller reporting company,” which would allow us to continue to take advantage of many of the same exemptions from disclosure requirements, including presenting only the two most recent fiscal years of audited financial statements and reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements. We may continue to be a smaller reporting company if either (i) the market value of our stock held by non-affiliates is less than \$250 million or (ii) our annual revenue is less than \$100 million during the most recently completed fiscal year and the market value of our stock held by non-affiliates is less than \$700 million. To the extent we take advantage of such reduced disclosure obligations, it may also make comparison of our financial statements with other public companies difficult or impossible.

## **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. If we are unable to obtain sufficient funding on a timely basis or on favorable terms, we may be required to significantly delay, alter reduce or eliminate one or more of our research or product development programs and/or commercialization efforts, or to grant rights to develop and market products or product candidates that we would otherwise prefer to develop and market ourselves. We may also be otherwise unable to execute our business plan or growth strategy, or capitalize on business opportunities as desired.

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, 2023, we had cash and cash equivalents of \$116.7 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, 2023, 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. In addition, we may have bank deposits at financial institutions in excess of FDIC insured limits. Market conditions can impact the viability of these institutions and, in the event of failure of the financial institution where we maintain our cash and cash equivalents, if the treatment of our cash sweep accounts were called into question in a bank receivership or if there is continued turmoil in the banking industry generally, we may not be able to access uninsured funds in a timely manner or at all, which would adversely impact our business, financial condition and results of operations. 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.

***Our failure to meet the continued listing requirements of The Nasdaq Capital Market could result in a delisting of our common stock.***

As previously disclosed, on April 24, 2023, we received a letter from Nasdaq (the "Nasdaq Notice") indicating that we were not in compliance with Nasdaq Listing Rule 5450(a)(1) because the closing bid price per share for our common stock was below \$1.00 for the previous 30 consecutive business days (the "Minimum Bid Price Requirement"). The Nasdaq Notice provided an initial period of 180 calendar days in which to regain compliance with the Minimum Bid Price Requirement by achieving a minimum bid price per share of our common stock of at least \$1.00 for at least ten consecutive business days.



On October 24, 2023, we received approval from the Listing Qualifications Department of Nasdaq to transfer the listing of our common stock from The Nasdaq Global Select Market to The Nasdaq Capital Market (the “Approval”). Our common stock was transferred to The Nasdaq Capital Market effective as of the open of business on October 26, 2023, and continues to trade under the symbol “DTIL.” The Nasdaq Capital Market operates in substantially the same manner as The Nasdaq Global Select Market, and listed companies must meet certain financial requirements and comply with Nasdaq’s corporate governance requirements. As a result of the Approval and transfer to The Nasdaq Capital Market, we were granted an additional 180-day grace period, or until April 22, 2024, to regain compliance with the Minimum Bid Price Requirement.

On January 18, 2024, our stockholders approved a proposal to amend our amended and restated certificate of incorporation to effect a reverse stock split of our common stock at a ratio of not less than 1-for-10 and not more than 1-for-30, with such ratio and the implementation and timing of such reverse stock split to be determined by our board of directors in its sole discretion. On February 6, 2024, our board of directors approved a 1-for-30 reverse stock split of our issued and outstanding common stock, and on February 13, 2024, we filed with the Secretary of State of the State of Delaware a certificate of amendment to our amended and restated certificate of incorporation in order to effect the reverse stock split. As a result of the reverse stock split, every 30 shares of our common stock issued or outstanding were automatically reclassified into one new share of common stock, and the number of our issued and outstanding shares of common stock was reduced to 4,191,053 and 4,164,038, respectively. Trading of our common stock on The Nasdaq Capital Market commenced on a split-adjusted basis on February 14, 2024. The primary goal of the reverse stock split was to increase the per share market price of our common stock to meet the Minimum Bid Price Requirement. All references to numbers of shares of common stock and per-share information in this Annual Report on Form 10-K have been adjusted retroactively, as appropriate, to reflect the reverse stock split.

On March 1, 2024, we were notified by Nasdaq Listing Qualifications that the closing bid price of our common stock had been \$1.00 per share or greater for 10 consecutive business days, from February 14, 2024 to February 29, 2024. Accordingly, we have regained compliance with the Minimum Bid Price Requirement. Although we regained compliance with the Minimum Bid Price Requirement, there can be no guarantee that we can continue to remain compliant or that we will be able to maintain compliance with the other Nasdaq listing standards.

Delisting our common stock may make it more difficult for us to raise capital on favorable terms in the future and would likely have a negative effect on the price of our common stock and would impair our stockholders’ ability to sell or purchase our common stock. In the event of a delisting, we can provide no assurance that any action taken by us to restore compliance with listing requirements would allow our common stock to become listed again, stabilize the market price or improve the liquidity of our common stock, prevent our common stock from dropping below the Minimum Bid Price Requirement or prevent future non-compliance with Nasdaq’s listing requirements. If for any reason our common stock does not maintain eligibility for listing on Nasdaq, we may list our common stock elsewhere, such as one of the over-the-counter markets, which are generally considered less liquid and more volatile than a national securities exchange, and could mean that certain institutional investors could no longer hold or purchase our stock, and as a result, a purchaser of our common stock may find it more difficult to dispose of, or to obtain accurate quotations as to the price of their shares. This could materially and adversely affect the liquidity of our common stock.

***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 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 1C. Cybersecurity.**

##### **Cybersecurity Risk Management and Strategy**

We have developed and implemented a cybersecurity risk management program intended to protect the confidentiality, integrity, and availability of our critical systems and information. Our cybersecurity risk management program includes a cybersecurity incident response plan.

We designed and assess our program based on the National Institute of Standards and Technology Cybersecurity Framework (“NIST CSF”). This does not imply that we meet any particular technical standards, specifications, or requirements, only that we use the NIST CSF as a guide to help us identify, assess, and manage cybersecurity risks relevant to our business.

We are utilizing our cybersecurity risk management program as the basis for developing our overall enterprise risk management program, and our current cybersecurity risk management program involves a range of policies, procedures, and controls designed to safeguard our information assets. Key elements of our cybersecurity risk management program include:

- risk assessments designed to help identify material cybersecurity risks to our critical systems, information, products, services, and our broader enterprise information technology environment;
- a security team principally responsible for managing (1) our cybersecurity risk assessment processes, (2) our security controls, and (3) our response to cybersecurity incidents;
- the use of external service providers, where appropriate, to assess, test, or otherwise assist with aspects of our security controls;
- cybersecurity awareness training for our employees, incident response personnel, and senior management;
- a cybersecurity incident response plan that includes procedures for responding to cybersecurity incidents; and
- a third-party risk management process for service providers, suppliers, and vendors that have access to our critical systems and information.

We have not identified risks from known cybersecurity threats, including as a result of any prior cybersecurity incidents, that have materially affected or are reasonably likely to materially affect us, including our operations, business strategy, results of operations, or financial condition. In addition, we have secured cyber insurance coverage, and we plan to regularly review our coverage to align with the evolving nature of cyber threats and industry standards. For more information, see the section titled “*Risk Factors— Our business and operations may suffer in the event of information technology system failures, cyberattacks or deficiencies in our security, which could materially affect our results.*” in Part I, Item 1A. of this Annual Report on Form 10-K.

## **Cybersecurity Governance**

Our board of directors considers cybersecurity risk part of its risk oversight function and has delegated to the audit committee of our board of directors (the “Audit Committee”) oversight of cybersecurity and other information technology risks. The Audit Committee oversees management’s implementation of our cybersecurity risk management program. The Audit Committee receives quarterly reports from the Vice President of Operation & Information Technology, and Head of Information Technology on our cybersecurity risks.

Our management team, including our Vice President of Operations & Information Technology and Head of Information Technology, has 18+ years of experience in enterprise risk management, governance, and technical operations, information technology enterprise architecture, and information technology management, and oversees our information security program. In addition, management regularly updates the Audit Committee with respect to cybersecurity risk, also on an ad hoc basis as necessary, regarding any material cybersecurity incidents and any incidents with lesser impact potential. The Audit Committee reports to the full board of directors regarding its activities, including those related to cybersecurity.

## **Item 2. Properties.**

We currently occupy approximately 71,305 square feet, with 11,890 square feet subleased, of office and laboratory space at our corporate headquarters in Durham, North Carolina under a lease that expires in 2029.

## **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 Capital Market under the symbol “DTIL.”

#### **Holders of Common Stock**

As of March 21, 2024, there were approximately 25 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 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.*

*A discussion regarding our financial condition and results of operation, including liquidity and capital resources, for the year ended December 31, 2023 compared to the year ended December 31, 2022 is presented below.*

### Overview

We are an advanced gene editing company dedicated to improving life by developing *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 for sophisticated gene edits, including gene insertion, excision, and elimination. 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.

### Business Updates

In August 2023, we completed a strategic transaction with Imugene Limited and its wholly-owned subsidiary Imugene (USA) Inc. (“Imugene US” and, together with Imugene Limited, “Imugene”) for our lead allogeneic chimeric antigen receptor (“CAR”) T candidate for cancer, azercabtagene zapreleucel (“azer-cel”). In exchange for global rights to azer-cel for cancer, as well as our CAR T infrastructure and experienced cell therapy team, we received upfront consideration valued at \$21 million, consisting of cash and convertible notes. We are eligible for an \$8 million milestone payment upon successful completion of the Phase 1b dosing in the CAR T relapsed large B cell lymphoma (“LBCL”) patient population, up to \$198 million in additional milestone payments and double-digit royalties on net sales of azer-cel, as well as \$145 million in milestone payments and tiered royalties for up to three additional research programs to be developed by Imugene. Imugene has assumed ongoing clinical execution for azer-cel in the LBCL population who have relapsed following CAR T treatment.

In January 2024, we entered into a license agreement with TG Cell Therapy, Inc. (“TG Subsidiary”) and its parent company TG Therapeutics, Inc. (“TG Parent” and, together with TG Subsidiary, “TG Therapeutics”) for non-oncological applications of azer-cel (the “TG License Agreement”). In connection with the TG License Agreement, we received upfront, and are also entitled to receive potential near-term economics, valued in the aggregate at \$17.5 million. The upfront payment was received on February 5, 2024 and is comprised of a (i) \$5.25 million cash payment and (ii) \$2.25 million cash payment in exchange for 97,360 shares of our common stock by TG Therapeutics at a price of \$23.10 per share, a 100% premium to the 30-day volume-weighted average price (“VWAP”) prior to the date of the TG License Agreement. We will also receive \$2.5 million within 12 months as an equity investment in our common stock at 100% premium to the then 30-day VWAP prior to purchase. Upon the achievement of certain near-term clinical milestones, we will receive an additional \$7.5 million payment in cash and the purchase of our common stock by TG Therapeutics at a 100% premium to the then current 30-day VWAP. We are eligible to receive up to \$288 million in additional milestone payments based on the achievement of certain clinical, regulatory, and commercial milestones, in addition to high-single-digit to low-double-digit royalties on net sales.

In February 2024, we announced that we had granted Caribou Biosciences, Inc. (“Caribou”), a leading CRISPR genome-editing cell therapy company, a non-exclusive, worldwide license, with the right to sublicense, to one of our foundational cell therapy patent families for use with CRISPR-based therapies in the field of human therapeutics. Under the terms of the agreement, we received an upfront payment and, upon commercialization by Caribou, will receive royalties on net sales of licensed products. In addition, for each occurrence of certain strategic transactions involving Caribou, we are entitled to receive a specific tiered milestone payment.

We are now solely focused on leveraging our proprietary ARCUS genome editing platform to advance *in vivo* gene editing programs that go beyond gene knockouts in the liver and carry out more sophisticated edits such as gene insertions, gene excision, and gene elimination, unlocking a broader potential for ARCUS *in vivo* gene editing in human therapeutics.

### Corporate Updates



We presented two poster presentations at the European Society of Gene & Cell Therapy (“ESGCT”) congress in October 2023, “Unique features of ARCUS nucleases enable high efficiency, targeted gene insertion *in vivo*” and “ARCUS-mediated excision of the “hot spot” region of the human dystrophin gene results in functional improvement in a mouse model of Duchenne muscular dystrophy (“DMD”).”

Our gene editing program PBGENE-HBV, for the potential treatment of chronic hepatitis B virus (“HBV”), remains a top priority, and we expect to submit an investigational new drug (“IND”) application or clinical trial application (“CTA”) in 2024. HBV causes inflammation and damage to the liver, leading to chronic infection and increased risk of death from liver cancer or cirrhosis. There is no cure for chronic hepatitis B and current treatments rarely result in functional cure, primarily due to persistence of viral DNA in the liver. In patients with chronic HBV, genetic material of the virus is converted within infected liver cells into covalently closed circular DNA (“cccDNA”) that acts as a template to make HBV copies. HBV also inserts its DNA into the human genome of infected liver cells. This integrated HBV DNA produces the viral protein, hepatitis B surface antigen (“HBsAg”), which is secreted in the blood. Presence of HBsAg is associated with poorer outcomes and elimination of HBsAg is necessary for functional cure of chronic hepatitis B.

PBGENE-HBV is designed to inactivate cccDNA with direct cuts and edits as well as to inactivate integrated HBV DNA with the goal of long-lasting reductions in HBsAg. We believe specificity is of particular importance for developing a safe gene editing approach to eliminating HBV, as a lack of nuclease specificity can lead to unfavorable off-target results including increased integrations of HBV genomes into the human genome, as well as translocations between integrations. Preclinical data from the PBGENE-HBV program was presented in April 2023 at an oral presentation at the Global Hepatitis Summit 2023, in June 2023 at an oral presentation at the European Association for Study of the Liver Congress 2023, and in November 2023 at the American Association for the Study of Liver Diseases Annual Meeting. Data highlighted that ARCUS nucleases exhibited high levels of on-target editing and demonstrated substantial reductions of both intracellular cccDNA and secreted HBsAg with no detectable translocations in primary human hepatocytes. In February 2024, we announced that we had received pre-IND regulatory feedback from the U.S. FDA in addition to regulatory feedback from agencies outside the U.S. providing clarity and alignment on PBGENE-HBV IND/CTA-enabling preclinical plans and clinical strategy.

At our R&D Day in September 2023, we announced that we intend to pursue development of PBGENE-PMM as a potential first-in-class opportunity for treatment of m.3243 associated primary mitochondrial myopathy (“PMM”). Mitochondrial diseases are the most common hereditary metabolic disorder, affecting 1 in 4,300 people. PMM currently lacks a curative treatment and impacts approximately 50% of patients with mitochondrial disease. The high specificity and single component nature of our mitoARCUS nucleases are designed to enable specific editing of mutant mitochondrial DNA while allowing normal (wild-type) mitochondrial DNA to repopulate in the mitochondria and restore normal function. Preclinical data from the PBGENE-PMM program presented in March 2024 at a poster presentation at the Mitochondrial Medicine – Therapeutic Development Annual Conference demonstrated ARCUS’ ability to efficiently eliminate mutant mitochondrial DNA without nuclear off-target editing. We expect to submit an IND and/or CTA application in 2025 with respect to PBGENE-PMM.

Also in September 2023, we received a Notice of Allowance from the U.S. Patent and Trademark Office (“USPTO”) for U.S. Patent Application No. 18/161,560, titled “Engineered Meganucleases That Target Human Mitochondrial Genomes.” The allowed patent includes composition of matter claims encompassing a mitochondria-targeted ARCUS nuclease (“mitoARCUS”) that is designed to specifically target, cleave, and eliminate mutant mitochondrial DNA comprising an m.3243A>G mutation.

We, along with our collaboration 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. In June 2023, we entered into an amended and restated development and license agreement (the “Prevail Agreement”) with Prevail Therapeutics, Inc. (“Prevail”), a wholly-owned subsidiary of Eli Lilly and Company. Pursuant to the terms of the Prevail Agreement, we and Prevail will continue to collaborate on developing our ARCUS nucleases for the research and development of potential *in vivo* therapies for genetic disorders, including DMD and two additional gene targets. We will continue to oversee creation, selection, *in vitro* development, and optimization of ARCUS nucleases with respect to the gene targets subject to the collaboration. Prevail will oversee and fund preclinical research and IND-enabling activities, which we previously were to conduct at our expense. We believe that shifting portions of the preclinical and IND-enabling activities on the collaboration targets to Prevail will allow us to further leverage our core capabilities in nuclease generation, development, and characterization for our internal wholly-owned programs. During the September 2023 R&D Day, we highlighted preclinical data demonstrating the potential of ARCUS *in vivo* gene editing for large gene excisions and that the edited dystrophin variant was observed in multiple tissue types frequently involved in progression of DMD, including skeletal muscle, heart, and diaphragm, thereby enabling significantly improved muscle function. We also shared data for another Prevail program during the R&D Day highlighting high efficiency gene insertion in adult non-human primates (“NHPs”).

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.

In partnership with iECURE, Inc. (“iECURE”), an ARCUS-mediated gene insertion approach is being pursued as a potential treatment option for neonatal onset ornithine transcarbamylase (“OTC”) deficiency. NHP 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 NHPs with high efficiency. iECURE received approval from the Australian Therapeutic Goods Administration for the initiation of a first-in-human Phase 1/2 trial evaluating ECUR-506, an investigational therapy incorporating an ARCUS nuclease in development for the treatment of OTC deficiency in pediatric (or neonatal) patients. In March 2024, iECURE also received approval from the U.K. Medicines & Healthcare products Regulatory Agency for the company’s CTA application to expand the Phase 1/2 OTC-HOPE study evaluating ECUR-506 into the U.K. iECURE is preparing sites and anticipates initiating the global clinical trial in the first half of 2024.

#### *Reverse Stock Split*

On January 18, 2024, our stockholders approved a proposal to amend our amended and restated certificate of incorporation to effect a reverse stock split of our common stock at a ratio of not less than 1-for-10 and not more than 1-for-30, with such ratio and the implementation and timing of such reverse stock split to be determined by our board of directors in its sole discretion. On February 6, 2024, our board of directors approved a 1-for-30 reverse stock split of our issued and outstanding common stock, and on February 13, 2024, we filed with the Secretary of State of the State of Delaware a certificate of amendment to our amended and restated certificate of incorporation in order to effect the reverse stock split. Trading of our common stock on The Nasdaq Capital Market commenced on a split-adjusted basis on February 14, 2024. As a result of the reverse stock split, every 30 shares of our common stock issued or outstanding were automatically reclassified into and became one new share of common stock, and the number of our issued and outstanding shares of common stock was reduced to 4,191,053 and 4,164,038, respectively. All references to numbers of shares of common stock and per-share information in this Annual Report on Form 10-K have been adjusted retroactively, as appropriate, to reflect the reverse stock split.

#### *Common Stock Offering*

In March 2024, we entered into an underwriting agreement relating to the issuance and sale of an aggregate of 2,500,000 shares of our common stock and warrants to purchase 2,500,000 shares of our common stock at a combined offering price of \$16.00 per share. Each warrant has an exercise price per share of \$20.00, is immediately exercisable and will expire on March 5, 2029. The offering was made pursuant to a registration statement on Form S-3.

### **License and Collaboration Transactions**

#### *TG Therapeutics*

On January 7, 2024, we entered into a license agreement (the “TG License Agreement”) with TG Cell Therapy, Inc. (“TG Subsidiary”) and its parent company TG Therapeutics, Inc. (“TG Parent” and, together with TG Subsidiary, “TG Therapeutics”), pursuant to which we granted TG Subsidiary certain exclusive and non-exclusive license rights to develop, manufacture, and commercialize azer-cel for autoimmune diseases and other indications outside of cancer pursuant to the terms of the TG License Agreement.

Under the TG License Agreement, we are entitled to receive an upfront cash payment of \$10.0 million (the “Upfront Payment”), an additional cash payment of \$7.5 million in the event that TG Therapeutics achieves a certain clinical milestone that is expected to be achieved in the near-term (the “Initial Milestone Payment”), and additional payments upon the achievement of additional specified milestones of up to \$288.6 million (the “Additional Milestone Payments”). As described below, up to \$10.0 million of the cash payments potentially payable us are payable in exchange for the issuance (the “Company Stock Issuances”) to TG Subsidiary of shares of our common stock.

The Upfront Payment of \$10.0 million is comprised of (i) a \$5.25 million cash payment that was paid to us on February 5, 2024, (ii) a \$2.25 million cash payment that was paid to us on February 5, 2024 payable in exchange for 97,360 shares of our common stock, based on a price per share equal to 200% of the VWAP of our common stock for the 30 trading days prior to the date of the TG License Agreement, and (iii) a deferred cash payment of \$2.5 million due within 12 months following the date of the TG License Agreement, payable in exchange for such number of shares of our common stock determined based on a price per share equal to the greater of (A) 200% of the VWAP of our common stock for the 30 trading days prior to the date of payment or (B) a minimum price of \$11.1660 determined in accordance with Nasdaq Listing Rule 5635(d) (the “Minimum Price”).

The Initial Milestone Payment of \$7.5 million, if payable, will consist of (i) a \$5.25 million cash milestone payment and (ii) a \$2.25 million cash payment payable in exchange for such number of shares of our common stock determined based on a price per share equal to the greater of (A) 200% of the VWAP of our common stock for the 30 trading days prior to the achievement of such milestone or (B) the Minimum Price.

The Additional Milestone Payments become due upon the achievement of certain milestones as specified in the TG License Agreement. Included within the Additional Milestone Payments is a potential payment of \$3.0 million in connection with achievement of a milestone specified in the TG License Agreement, payable in exchange for such number of shares of our common stock determined based on a price per share equal to the greater of (A) 200% of the VWAP of our common stock for the 30 trading days prior to the achievement of such milestone or (B) the Minimum Price.

Subject to the terms and conditions of the TG License Agreement, TG Therapeutics is permitted to pay up to 50% of the value of each Additional Milestone Payment (other than the Additional Milestone Payment described above that would, upon achievement, involve the issuance of \$3.0 million of Shares by Precision) in freely tradable shares of common stock of TG Parent, valued based on the VWAP of the TG Parent shares of common stock on Nasdaq for the 30 trading days prior to the achievement of the applicable milestone.

If a licensed product under the TG License Agreement is approved and sold, TG Therapeutics is also required to pay us tiered royalties ranging from high-single-digit to low-double-digit percentages on net sales of the licensed product. TG Therapeutics' 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 (i) the expiration of the last-to-expire valid claim in such country covering such licensed product; (ii) the expiration of any period of data, regulatory, or market exclusivity, or supplemental protection certificates (other than patents) covering the licensed product in such country; and (iii) a period of ten years following the first commercial sale of the respective licensed product in such country.

Unless earlier terminated, the TG License Agreement will remain in effect on a licensed product-by-licensed product and country-by-country basis until the expiration of a defined royalty term for each licensed product and country. We may terminate the TG License Agreement if TG Therapeutics fails to initiate certain development activities with respect to the licensed product by a specified date or ceases active development of the licensed product for a specified period of time. In addition, we may terminate the TG License Agreement if TG Therapeutics or any of its affiliates or sublicensees challenges the validity of any patents controlled by us. We or TG Therapeutics may terminate the TG License Agreement (i) for material breach by the other party and a failure to cure such breach within the time period specified in the TG License Agreement or (ii) the other party's insolvency.

#### *Sale of CAR T Platform to Imugene*

On August 15, 2023 we entered into an asset purchase agreement with Imugene (the "Imugene Purchase Agreement"). Pursuant to and simultaneously with the execution of the Imugene Purchase Agreement, on August 15, 2023 (the "Closing Date"), Imugene US acquired our manufacturing infrastructure used in the development and manufacture of azer-cel, including assuming the lease to our manufacturing facility and certain contracts with respect to our manufacturing facility, and related equipment, supplies, azer-cel clinical trial inventory and other assets related to our CAR T cell therapy platform (the "Acquired Assets"). As part of the Imugene Purchase Agreement, Imugene US hired a number of the Company's employees who were associated with our historical CAR T cell therapy operations.

In consideration for the Acquired Assets, Imugene US assumed certain liabilities, paid us \$8 million in cash, and issued us convertible notes pursuant to the terms and conditions set forth in a convertible note subscription deed (collectively, the "Imugene Convertible Note") in an aggregate principal amount of \$13 million. The Imugene Convertible Note is non-interest bearing and matures on the first anniversary of the Closing Date (the "Maturity Date"). On the Maturity Date, the Imugene Convertible Note will be redeemed with cash, converted into ordinary shares of Imugene Limited at a conversion price based on the 10-day volume weighted average price of Imugene Limited's ordinary shares prior to the date of conversion, or partially redeemed with cash and partially converted into shares, at Imugene's discretion.

Additionally, we entered into a license agreement with Imugene (the "Imugene License Agreement") on the Closing Date, pursuant to which we granted Imugene US certain exclusive and non-exclusive license rights to develop, manufacture, and commercialize oncological applications of our allogeneic CAR T therapy, azer-cel, and up to three additional research product candidates directed to targets that Imugene US may nominate prior to the fifth anniversary of the effective date of the Imugene License Agreement, pursuant to the terms of the Imugene License Agreement.

In addition, under the License Agreement, we are eligible to receive milestone payments of up to an aggregate of \$206 million for azer-cel, inclusive of a payment of \$8 million in cash and equity upon successful completion of the Phase 1b dosing in the CAR T

relapsed LBCL patient population. For azer-cel, we are eligible to receive double-digit royalties on net sales. For up to three additional research programs to be developed by Imugene, we are eligible for up to \$145 million in milestone payments and, if licensed products are approved and sold, tiered royalties ranging from the mid-single digit to low-double digit percentages on net sales of such licensed products. In addition, we are eligible to receive mid-single digit percentage-based fees for certain change of control transactions involving Imugene and for partnering transactions involving a licensed product. Imugene'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 respective licensed product.

Unless earlier terminated, the Imugene License Agreement will remain in effect on a licensed product-by-licensed product and country-by-country basis until the expiration of a defined royalty term for each licensed product and country. We may terminate the entire Imugene License Agreement due to a challenge to our patents brought by Imugene and a breach by Imugene in any material respect of the Imugene License Agreement, the Imugene Purchase Agreement or any related transaction documents. We may also terminate the Imugene License Agreement with respect to azer-cel if Imugene fails to initiate certain development activities with respect to azer-cel by a specified date, if Imugene fails to expend certain amounts on the development of azer-cel or if Imugene ceases active development of azer-cel for a specified period of time. Either party may terminate the Imugene License Agreement (i) for material breach by the other party and a failure to cure such breach within the time period specified in the agreement or (ii) the other party's insolvency.

In connection with the Imugene Purchase Agreement and the Imugene License Agreement, we and Imugene have entered into other related agreements and documents, including a registration rights agreement, a transition services agreement, a sublease for laboratory space at our headquarters and a parent company guaranty from Imugene Limited.

We concluded the Imugene License Agreement represents functional intellectual property in accordance with ASC 606 given we do not expect to provide any additional services to Imugene outside of the right to use the licensed intellectual property. As of December 31, 2023 management has constrained all variable consideration related to milestone payments in the Imugene License Agreement given the level of uncertainty associated with achievement of the milestone payments. Accordingly, no revenue was recognized under the Imugene License Agreement during the year ended December 31, 2023.

#### *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 (collectively referred to as licensed products). Any initial licensed products under the Novartis Agreement 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 413,581 shares of our common stock (the "Novartis Shares") in a private placement transaction for an aggregate purchase price of \$25.0 million, or approximately \$60.30 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 years ended December 31, 2023 and 2022 we recognized revenue under the Novartis Agreement of \$22.7 million and \$9.5 million, respectively. Deferred revenue related to the Novartis Agreement amounted to \$32.4 million and \$54.2 million as of December 31, 2023 and December 31, 2022, respectively, of which \$7.4 million and \$27.9 million, respectively, was included in current liabilities within the balance sheets.

#### *Prevail Therapeutics, Inc.*

On November 19, 2020, we entered into a development and license agreement with Eli Lilly and Company (“Lilly”) to collaborate to discover and develop *in vivo* gene editing products incorporating our ARCUS nucleases to utilize ARCUS for the research and development of potential *in vivo* therapies for genetic disorders. This agreement was subsequently assigned to Prevail Therapeutics, a wholly-owned subsidiary of Lilly, effective November 1, 2022 (the “Original Prevail Agreement”).

On June 30, 2023, we entered into the Prevail Agreement which amended and restated the Original Prevail Agreement. Pursuant to the terms of the Prevail Agreement, we and Prevail will continue to collaborate on developing our ARCUS nucleases for the research and development of potential *in vivo* therapies for genetic disorders, including DMD, a liver-directed target, and a central nervous system directed target. Prevail also continues to have the right to nominate up to three additional gene targets for genetic disorders over the initial nomination period of four years. Prevail may extend the nomination period for an additional two years from the date on which such initial nomination period ends, upon Prevail’s election and payment of an extension fee. Additionally, Prevail has the option to replace up to two gene targets upon Prevail’s election and payment of a replacement target fee.

Prevail will oversee and fund preclinical research and IND-enabling activities following creation, selection, *in vitro* development, and optimization of ARCUS nucleases with respect to the gene targets subject to the collaboration, which were previously conducted by us at our expense. Manufacturing initial clinical trial material for the first licensed product, which was previously our responsibility to conduct at Prevail’s expense, will instead be Prevail’s responsibility at Prevail’s expense. Prevail will continue to 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.

In connection with the closing of the original development and license agreement with Lilly, we received an upfront cash payment of \$100.0 million as well as \$35.0 million from Lilly’s purchase of 125,406 newly issued shares of our common stock. Under the Prevail Agreement, we will also be eligible to receive milestone payments of up to an aggregate of \$390 million to \$395 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. Prevail'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.

During the years ended December 31, 2023 and 2022, we recognized revenue under the Prevail Agreement of \$26.0 million and \$15.6 million, respectively. Deferred revenue related to the Prevail Agreement was \$52.7 million and \$74.8 million as of December 31, 2023 and December 31, 2022, respectively, of which \$4.7 million and \$18.3 million, respectively, was included in current liabilities within the balance sheets.

### *iECURE*

In August 2021, we entered into a development and license agreement with iECURE (the "iECURE DLA") under which iECURE was to advance our PBGENE-PCSK9 candidate through preclinical activities as well as a Phase 1 clinical trial in order to gain access to a license to use our PCSK9-directed ARCUS nuclease to insert genes into the PCSK9 locus to develop treatments for four pre-specified rare genetic diseases, including OTC deficiency (the "PCSK9 License"). Simultaneously with the entry into the iECURE DLA, we and iECURE entered into an equity issuance agreement (the "iECURE Equity Agreement"), pursuant to which iECURE issued us common stock in iECURE as additional consideration for the PCSK9 license. Additionally, we are eligible to receive milestone and mid-single digit to low double digit royalty payments on sales of iECURE products developed with ARCUS.

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). During the year ended December 31, 2023, we recorded a \$0.6 million increase in the carrying value of our iECURE equity to adjust to fair value.

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") were recorded to the prepaid expenses and other assets line items of the 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. During the year ended December 31, 2022, we recognized \$2.1 million of research and development expense related to amortization of the PCSK9 Prepaid. The remaining unamortized PCSK9 Prepaid was fully impaired during the year ended December 31, 2022 as we made the decision to cease pursuit of PBGENE-PCSK9 for familial hypercholesterolemia with iECURE as our partner in December 2022. Accordingly, there was no PCSK9 Prepaid balance as of December 31, 2023 or 2022.

## **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, 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 third parties that conduct preclinical research and development activities on our behalf;
- costs of manufacturing drug products for use in our preclinical studies, including the costs of contract manufacturing organizations ("CMOs");
- costs of outside consultants;
- costs of laboratory supplies and acquiring, developing and manufacturing preclinical study materials;
- license payments made for intellectual property used in research and development activities; and
- facility-related expenses, which include direct depreciation costs and expenses for rent and maintenance of facilities and other operating costs if specifically identifiable to research activities.

We expense research and development costs as incurred. We track external research and development costs by product candidate beginning when it is publicly named as a development program. Internal and external costs that are not identifiable to specific development candidates are included in the platform development 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 progress development of our product candidates.

We cannot determine with certainty the duration and costs of future clinical trials for our product candidates 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 product candidates will depend on a variety of factors, including:

- the scope, rate of progress, expense and results of future clinical trials of our product candidates and other research and development activities that we may conduct;
- the ability to collaborate and partner with third parties to fund any or all of our programs;
- 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, consulting fees, recruitment-related costs and other employee-related costs, including share-based compensation, for personnel in our executive, finance, business development, operations and administrative functions. General and administrative expenses also include legal fees relating to intellectual property and corporate matters; information technology costs; insurance costs; travel expenses; and facility-related expenses, which include direct depreciation costs and expenses for rent and maintenance of facilities and other operating costs that are not specifically attributable to research activities.

#### *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 is 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 and impairment recognized on assets held for sale.

#### *Gain (Loss) on Changes in Fair Value*

The change in fair value of represents the assessed changes in fair value of assets and liabilities carried at fair value.

#### *Loss from Equity Method Investment*

Loss from equity method investment represents our proportionate share of the net loss of our equity method investee, Elo Life Systems, Inc. (“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 from Elo.

### *Loss from Discontinued Operations*

Loss from discontinued operations represents the gain on the sale of our CAR T infrastructure to Imugene and the results of operations of our historical cell therapy operations.

## **Results of Operations**

### *Comparison of the Years Ended December 31, 2023 and December 31, 2022*

The following table summarizes our results of operations for the years ended December 31, 2023 and December 31, 2022, together with the changes in those items in dollars:

(in thousands)	Years ended December 31,		Change
	2023	2022	
Revenue	\$ 48,727	\$ 25,098	\$ 23,629
Operating expenses:			
Research and development	53,375	46,122	7,253
General and administrative	39,088	41,284	(2,196)
Total operating expenses	<u>92,463</u>	<u>87,406</u>	<u>5,057</u>
Loss from operations	(43,736)	(62,308)	18,572
Other income (expense), net:			
Impairment charges	—	(10,844)	10,844
Loss on disposal of assets	(461)	(30)	(431)
Gain (loss) on changes in fair value	1,145	(510)	1,655
Loss from equity method investment	(4,931)	(1,579)	(3,352)
Interest expense	(2,230)	(1,111)	(1,119)
Interest income	<u>7,686</u>	<u>3,473</u>	<u>4,213</u>
Total other income (expense), net	<u>1,209</u>	<u>(10,601)</u>	<u>11,810</u>
Loss from continuing operations	<u>(42,527)</u>	<u>(72,909)</u>	<u>30,382</u>
Loss from discontinued operations (including gain on disposal of \$8,446 during the year ended December 31, 2023)	<u>(18,792)</u>	<u>(38,728)</u>	<u>19,936</u>
Net loss	<u>\$ (61,319)</u>	<u>\$ (111,637)</u>	<u>\$ 50,318</u>

### *Revenue*

Revenue for the year ended December 31, 2023 was \$48.7 million, compared to \$25.1 million for the year ended December 31, 2022. The increase of \$23.6 million in revenue during the year ended December 31, 2023 was primarily the result of a \$10.4 million increase in revenue recognized under the Prevail Agreement. On June 30, 2023, we amended the Original Prevail Agreement, which resulted in a decrease in total estimated effort required to satisfy the performance obligation under the agreement, as so amended and restated, and an increase in the transaction price.

Also contributing to the increase in revenue was an increase of \$13.2 million in revenue recognized under the Novartis Agreement as 2023 was the first full year of revenue recognized under the Novartis Agreement.

## Research and Development Expenses

(in thousands)	Years ended December 31,		Change
	2023	2022	
Direct research and development expenses by product candidate:			
PBGENE-HBV external development costs	9,261	804	8,457
PBGENE-PMM external development costs	352	—	352
Platform development and early-stage research expenses:			
Employee-related costs (other than share based compensation)	19,788	18,732	1,056
Share based compensation	3,642	5,410	(1,768)
Laboratory supplies and services	5,741	8,585	(2,844)
Outsourced research and development	4,682	3,458	1,224
CMOs and research organizations	71	45	26
Laboratory equipment and maintenance	938	1,049	(111)
Facility-related costs	2,370	2,053	317
Depreciation and amortization	4,022	4,010	12
Licensing fees	2,468	1,968	500
Other research and development costs	40	8	32
<b>Total research and development expenses</b>	<b>\$ 53,375</b>	<b>\$ 46,122</b>	<b>\$ 7,253</b>

Research and development expenses for the year ended December 31, 2023 were \$53.4 million, compared to \$46.1 million for the year ended December 31, 2022. The increase of \$7.3 million was primarily due to an \$8.5 million increase in PBGENE-HBV external development costs related to CTA/IND-enabling studies. Also contributing to the increase was a \$1.2 million increase in outsourced research and development costs primarily related to consulting fees, a \$1.1 million increase in employee-related costs (other than share based compensation) as a result of increases in performance based compensation, a \$0.5 million increase in licensing fees, and a \$0.3 million increase in facility-related costs. Additionally, PBGENE-PMM external development costs increased by \$0.4 million as we began pursuing development of PBGENE-PMM during the year ended December 31, 2023.

Partially offsetting the increases in research and development expenses was a \$2.8 million decrease in laboratory supplies and services expenses primarily related to a decrease in expense related to partnered programs. Additionally share based compensation expenses decreased \$1.8 million due to forfeitures.

## General and Administrative Expenses

General and administrative expenses were \$39.1 million for the year ended December 31, 2023 compared to \$41.3 million for the year ended December 31, 2022. The decrease of \$2.2 million was primarily due to a \$1.5 million decrease in share-based compensation expense and a \$0.7 million decrease in insurance expense driven by a market-related reduction in director and officer insurance premiums.

## Impairment Charges

There were no impairment charges during the year ended December 31, 2023. Impairment charges were \$10.8 million during the year ended December 31, 2022 which is comprised of the \$10.8 million impairment of the iECURE PCSK9 Prepaid as we 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.

## Loss on Disposal of Assets

Loss on disposal of assets was \$0.5 million during the year ended December 31, 2023 which included the proceeds from sales of equipment less the remaining net book value at the time of the equipment's disposal and impairment losses recognized on assets held for sale. Loss on disposal of assets was less than \$0.1 million for the year ended December 31, 2022 which represented the remaining net book value at the time of the equipment's disposal.

## Gain (Loss) on Changes in Fair Value

Gain from changes in fair value was \$1.1 million for the year ended December 31, 2023, which is primarily the result of an increase in the assessed fair value of the iECURE equity investment as iECURE has progressed towards a clinical trial for OTC deficiency. 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.

#### *Loss from Equity Method Investment*

Loss from equity method investment was \$4.9 million during the year ended December 31, 2023 and represented our proportionate share of Elo's net loss for such period. Loss from equity method investment was \$1.6 million during the year ended December 31, 2022 and represented our proportionate share of Elo's net loss for such period, partially offset by a gain recorded from an increase in our proportionate share of Elo's net assets resulting from an equity issuance by Elo.

#### *Interest Expense*

Interest expense was \$2.2 million for the year ended December 31, 2023 compared to \$1.1 million during the year ended December 31, 2022. The \$1.1 million increase in interest expense was primarily the result of a higher average balance on our debt and with higher interest rates during the year ended December 31, 2023 as compared to the year ended December 31, 2022.

#### *Interest Income*

Interest income was \$7.7 million during the year ended December 31, 2023 compared to \$3.5 million during the year ended December 31, 2022. The \$4.2 million increase in interest income was primarily driven by higher interest rates on our cash and cash equivalents during the year ended December 31, 2023 as compared to the year ended December 31, 2022.

#### *Loss from Discontinued Operations*

Loss from discontinued operations was \$18.8 million during the year ended December 31, 2023 compared to \$38.7 million during the year ended December 31, 2022. The \$19.9 million decrease in loss from discontinued operations was the result of the \$8.4 million gain on sale of our CAR T infrastructure to Imugene and a \$11.5 million decrease in cell therapy expenses during the year ended December 31, 2023 as compared to the year ended December 31, 2022.

#### *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, 2023, we had federal and state NOL carryforwards of \$195.0 million and \$166.8 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, 2023, we also had federal and state R&D tax credits of \$17.2 million and an amount less than \$0.1 million, which begin to expire in 2029 and 2030, respectively. As of December 31, 2023 we had federal Orphan Drug credits of \$13.5 million which begin to expire in 2038. As of December 31, 2023, we also have federal contribution carryforwards of \$0.2 million, which began to expire in 2023. We have recorded a full valuation allowance against our net deferred tax assets at each balance sheet date.

### **Liquidity and Capital Resources**

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 incurred significant operating losses since our inception 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 or other licensees for which we may receive milestone payments or royalties. As of December 31, 2023, we had an accumulated deficit of \$489.6 million.

We expect to incur significant expenses and operating losses for the foreseeable future as we advance the development of our product candidates. We expect that our research and development and general and administrative costs will increase over the long term, including in connection with conducting preclinical studies and potential clinical trials for our product candidates, contracting with CROs and CMOs, expanding our intellectual property portfolio and providing general and administrative support for our operations. 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. 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, 2023, we had cash and cash equivalents of \$116.7 million and available borrowings under our loan and security agreement (as amended from time to time, the “Revolving Line”) with Pacific Western Bank (“PWB”) of \$7.5 million. Covenants on our Revolving Line require that we maintain an aggregate balance of unrestricted cash at PWB (not including amounts in certain specified accounts) equal to or greater than \$10.0 million. Our sources of funding to finance our cash needs include proceeds from third parties through a combination of financings including our initial public offering (“IPO”), preferred stock and convertible note financings, underwritten offerings of our common stock, ATM offerings of our common stock as part of our shelf registration statement, upfront and milestone payments from partners, borrowings under bank facilities and funding from other strategic alliances and grants.

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 current global macroeconomic conditions. If we are unable to obtain sufficient financing on a timely basis or on favorable terms, we may be required to significantly delay, alter reduce or eliminate one or more of our research or product development programs and/or commercialization efforts, or to grant rights to develop and market products or product candidates that we would otherwise prefer to develop and market ourselves. We may also be otherwise unable to execute our business plan or growth strategy, or capitalize on business opportunities as desired. Any of these events could materially adversely affect our financial condition and business prospects.

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, potentially 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 operations.

#### *Cash Flows*

Our cash and cash equivalents totaled \$116.7 million and \$189.6 as of December 31, 2023, and 2022, respectively.

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

(in thousands)	For the Years Ended December 31,	
	2023	2022
Net cash used in operating activities	\$ (84,114)	\$ (45,753)
Net cash provided by (used in) investing activities	5,829	(3,319)
Net cash provided by financing activities	5,387	94,985
(Decrease) increase in cash and cash equivalents	\$ (72,898)	\$ 45,913

We experienced a decrease in cash and cash equivalents during the year ended December 31, 2023 of \$72.9 million, compared to a \$45.9 million increase in cash and cash equivalents during the year ended December 31, 2022. The \$118.8 million decrease in cash flows in the comparable periods was primarily due to the year over year decrease in net cash provided by financing activities and an increase in cash used in operating activities.

#### *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 costs. The use of cash in operating activities during the years ended December 31, 2023 and December 31, 2022 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, 2023 was \$84.1 million, compared to \$45.8 million during the year ended December 31, 2022. The \$38.3 million increase in cash used in operating activities was primarily driven by the \$50.0 million upfront payment received from Novartis pursuant to the terms of the Novartis Agreement during the year ended December 31, 2022.

#### *Cash Provided by (Used in) Investing Activities*

Cash provided by investing activities relates to proceeds received from disposed assets. Cash used in investing activities primarily relates to cash expenditures to acquire leasehold additions, equipment, software and intangible assets. Net cash provided by investing

activities during the year ended December 31, 2023 was \$5.8 million, compared to \$3.3 million net cash used in investing activities during the year ended December 31, 2022. The \$9.1 million net increase in cash provided by investing activities was primarily driven by \$8.0 million in proceeds received from Imugene as partial consideration for assets acquired under the Purchase Agreement and a \$1.4 million decrease in cash paid to purchase property, equipment and software during the year ended December 31, 2023 compared to the year ended December 31, 2022.

#### *Cash Provided by Financing Activities*

Net cash provided by financing activities during the year ended December 31, 2023 was \$5.4 million, compared to \$95.0 million during the year ended December 31, 2022. The \$89.6 million decrease in cash provided by financing activities during the year ended December 31, 2023 was primarily due a \$44.0 million decrease in common stock issuance proceeds, \$25.0 million in proceeds from the Novartis Stock Purchase Agreement in June 2022, and \$20.0 million in borrowings from our revolving credit facility in May 2022.

#### *Debt Obligations*

##### **Revolving Line**

We may request advances on our Revolving Line with PWB up to an aggregate principal amount of \$30.0 million. The Revolving Line maturity date is June 23, 2024 and 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, 2023, the outstanding principal balance on the Revolving Line was \$22.5 million, the stated interest rate was 9.25% and the effective interest rate was 10.3%.

#### *Funding Requirements*

We will continue to have funding requirements in connection with the continuation of our research and development efforts, potential IND and CTA submissions, potential clinical trials, and expected growth in our *in vivo* portfolios.

We believe that, as of the date of this Annual Report on Form 10-K, existing cash and cash equivalents, expected operational receipts, including near-term consideration to be received from licensees, operational efficiencies gained from divestment of our historical CAR T operations, and availability of our ATM facility will be sufficient to fund our operating expenses and capital expenditure requirements into the second half of 2026. We expect our cash runway to be sufficient to achieve first-in-human Phase 1 clinical data for our lead *in vivo* gene editing programs. 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 ability to collaborate and partner with third parties to fund any or all of our programs;
- the progress, costs and results of our additional research and preclinical development programs including our *in vivo* pipeline and our planned IND or CTA submissions and potential BLA submissions;
- the outcome, timing and cost of meeting regulatory requirements established by the FDA and other comparable foreign regulatory authorities;
- 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, our stockholders’ 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 significantly delay, alter reduce or eliminate one or more of our research or product development programs and/or commercialization efforts, or to grant rights to develop and market products or product candidates that we would otherwise prefer to develop and market ourselves. We may also be otherwise unable to execute our business plan, growth strategy, or capitalize on business opportunities as desired.

### *Common Stock Offering*

In March 2024, we entered into an underwriting agreement relating to the issuance and sale of an aggregate of 2,500,000 shares of our common stock and warrants to purchase 2,500,000 shares of our common stock at a combined offering price of \$16.00 per share. Each warrant has an exercise price per share of \$20.00, is immediately exercisable and will expire on March 5, 2029. The offering was made pursuant to a registration statement on Form S-3. Gross proceeds from the transaction were \$40.0 million before deducting underwriting discounts and commissions and offering expenses of approximately \$2.9 million. In addition, we granted the underwriters a 30-day option to purchase up to an additional 375,000 shares of its common stock at \$16.00 per share, less underwriting discounts and commissions. We intend to use the net proceeds of the offering to fund ongoing and planned research and development, and for working capital and other general corporate purposes.

### **Contractual Obligations and Commitments**

In addition to the contractual obligations and commitments as described elsewhere in this Annual Report on Form 10-K with respect to leases, the Revolving Line, and intellectual property licenses, we also enter into contracts in the normal course of business with CMOs, universities, and other third parties for preclinical research studies, testing, manufacturing services, and other services and products for operating purposes. These contract are generally cancelable upon written notice.

The Company does not have any material capital expenditure commitments at December 31, 2023.

### **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 (i) licenses, or options to obtain licenses, to use our technology, (ii) research and development activities to be performed on behalf of the collaborative partner, and (iii) 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 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 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 balance sheets.

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

**Royalties** – For arrangements that include sales-based royalties, including milestone payments based on a level of sales, which are the result of a customer-vendor relationship and for which the license is deemed to be the predominant item to which the royalties relate, we recognize revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied or partially satisfied. To date, we have not recognized any royalty revenue resulting from any of our licensing arrangements.

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

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

We analyze our collaboration arrangements to assess whether they are within the scope of 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 the year ended December 31, 2023, we recorded cumulative catch up adjustments that increased revenue by \$7.6 million related to the Prevail Agreement and decreased revenue by \$6.0 million related to the Novartis Agreement as a result of changes in total estimated effort required to satisfy performance obligations and changes in variable consideration included in the transaction price related to estimated fees to be received from partners. 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 \$8.6 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 \$10.5 million in the current year.

### ***Accrued Research and Development Expenses***

As part of the process of preparing our 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 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:

- 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 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**

Accounting standards updates that have been issued, but are not effective until after December 31, 2023, are not expected to have a material effect on our financial position, statements of operations or cash flows.

## **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.

## **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 \$116.7 million, or 73% of our total assets, on December 31, 2023 and \$189.6 million, or 80% of our total assets, on December 31, 2022. Interest income earned on our assets was \$7.7 million and \$3.5 million for the years ended December 31, 2023 and December 31, 2022, 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, 2023.

## **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, 2023.

## **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, 2023, 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 a non-accelerated filer as defined in the Exchange 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, 2023 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 February 29, 2024:

Name	Age	Position at Precision BioSciences, Inc.	Principal Employment
<b>Executive Officers</b>			
Michael Amoroso	46	President, Chief Executive Officer and Director	Same
John Alexander Kelly	57	Chief Financial Officer	Same
Alan List, M.D.	69	Chief Medical Officer	Same
Dario Scimeca	48	General Counsel and Secretary	Same
Jeff Smith, Ph.D.	50	Chief Research Officer	Same
<b>Non-Employee Directors</b>			
Kevin Buehler	66	Chair of the Board and Director	Former Division Head of Alcon Laboratories, Inc. a division of Novartis AG
Melinda Brown	67	Director	Former Senior Vice President and Controller of Tapestry, Inc.
Stanley Frankel, M.D.	65	Director	Former Chief Medical Officer of Cytovia Therapeutics, Inc.
Geno Germano	63	Director	President, Chief Executive Officer and Director of Elucida Oncology, Inc.
Shari Lisa Piré, J.D.	59	Director	Chief Legal & Sustainability Officer at Plume Design, Inc.
Sam Wadsworth, Ph.D.	75	Director	Senior Scientific Advisor of Ultragenyx Pharmaceuticals, Inc.

#### Insider Trading Arrangements and Policies

We are committed to promoting high standards of ethical business conduct and compliance with applicable laws, rules and regulations. As part of this commitment, we have adopted our Insider Trading Policy governing the purchase, sale, and/or other dispositions of our securities by our directors, officers, and other employees, as well as by the Company itself, that we believe is reasonably designed to promote compliance with insider trading laws, rules and regulations, and the exchange listing standards applicable to us. A copy of our Insider Trading Policy is filed as Exhibit 19.1 to this Annual Report on Form 10-K.

The remaining information required by this item will be included in our definitive proxy statement (“2024 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 2024 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 2024 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 2024 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 2024 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-32 attached hereto and are filed as part of this Annual Report on Form 10-K.

#### INDEX TO FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm (PCAOB ID: 34)	F-1
Balance Sheets as of December 31, 2023 and December 31, 2022	F-3
Statements of Operations for the Years Ended December 31, 2023 and December 31, 2022	F-5
Statements of Changes in Stockholders' Equity for the Years Ended December 31, 2023 and December 31, 2022	F-6
Statements of Cash Flows for the Years Ended December 31, 2023 and December 31, 2022	F-7
Notes to Financial Statements	F-8

#### (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
2.1 <sup>††</sup>	Asset Purchase Agreement, dated as of August 15, 2023, by and among Precision BioSciences, Inc., Imugene (USA) Inc. and Imugene Limited.	8-K/A	001-38841	2.1	8/21/2023	
3.1	Amended and Restated Certificate of Incorporation of Precision BioSciences, Inc.	8-K	001-38841	3.1	4/1/2019	
3.2	Certificate of Amendment to the Amended and Restated Certificate of Incorporation of Precision BioSciences, Inc.	8-K	001-38841	3.1	2/13/2024	
3.3	Amended and Restated Bylaws of Precision BioSciences, Inc.	8-K	001-38841	3.1	12/22/2023	
4.1	Specimen Common Stock Certificate.	S-1/A	333-230034	4.1	3/18/2019	
4.2	Amended and Restated Investors' Rights Agreement, dated May 25, 2018, as amended, by and among Precision BioSciences, Inc. and certain of its stockholders and the holders of the 2019 Notes,	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, dated May 25, 2018, as amended, by and among Precision BioSciences, Inc. and certain of its stockholders and the holders of the 2019 Notes.	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	Form of Warrant.	8-K	001-38841	4.1	3/1/2024	
4.6	Description of Registrant's Securities.					*
10.1 <sup>†††</sup>	Loan and Security Agreement, dated May 15, 2019, by and among Precision BioSciences, Inc., Elo Life Systems, Inc. and Pacific Western Bank, as amended.	10-K	001-38841	10.1	3/9/2023	
10.2 <sup>†††</sup>	License Agreement by and among TG Therapeutics, Inc., TG Cell Therapy, Inc. and Precision BioSciences, Inc.					*
10.3 <sup>†††</sup>	License Agreement, effective as of August 15, 2023 by and between Precision BioSciences, Inc. and Imugene (USA) Inc.	8-K/A	001-38841	10.1	8/21/2023	
10.4 <sup>††</sup>	Program Purchase Agreement, dated April 9, 2021, by and among Les Laboratoires Servier, Institut de Recherches Internationales Servier, and Precision BioSciences, Inc.	10-Q	001-38841	10.1	5/13/2021	
10.5 <sup>†††</sup>	Amended and Restated Development and License Agreement, dated June 30, 2023, by and between Prevail Therapeutics, Inc. and Precision BioSciences, Inc.	8-K	001-38841	10.1	7/6/2023	
10.6	Stock Purchase Agreement, dated November 19, 2020, by and between Eli Lilly and Company and Precision BioSciences, Inc.	10-K	001-38841	10.6	3/18/2021	
10.7 <sup>†††</sup>	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	
10.8 <sup>†††</sup>	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	
10.9	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	
10.10 <sup>†</sup>	License Agreement, dated April 17, 2006, as amended, by and between Duke University and Precision BioSciences, Inc.	S-1	333-230034	10.2	3/1/2019	
10.11 <sup>†</sup>	Patent Cross License Agreement, dated January 23, 2014, by and between Collectis SA and Precision BioSciences, Inc.	S-1	333-230034	10.3	3/1/2019	
10.12	Lease Agreement, dated April 5, 2010, as amended, by and between Precision BioSciences, Inc. and Venable Tenant, LLC.					*

<u>Exhibit Number</u>	<u>Description</u>	<u>Form</u>	<u>File No.</u>	<u>Exhibit</u>	<u>Filing Date</u>	<u>Filed Herewith</u>
10.13 <sup>#</sup>	2006 Stock Incentive Plan, as amended, and form of award agreements thereunder.	S-1	333-230034	10.8	3/1/2019	
10.14 <sup>#</sup>	2015 Stock Incentive Plan, as amended, and form of award agreements thereunder.	S-1	333-230034	10.9	3/1/2019	
10.15 <sup>#</sup>	2019 Incentive Award Plan, and forms of award agreements thereunder.	10-K	001-38841	10.14	3/18/2021	
10.16 <sup>#</sup>	2019 Employee Stock Purchase Plan.	S-1/A	333-230034	10.11	3/18/2019	
10.17 <sup>#</sup>	2021 Employment Inducement Incentive Award Plan and form of award agreements thereunder.	S-8	333-259369	99.3	9/7/2021	
10.18 <sup>#</sup>	Amendment to the Precision BioSciences, Inc. 2021 Employment Inducement Incentive Award Plan.	S-8	333-267079	99.4	8/26/2022	
10.19 <sup>#</sup>	Executive Employment Agreement, dated January 22, 2024, by and between Alex Kelly and Precision BioSciences, Inc.	8-K	001-38841	10.2	1/23/24	
10.20 <sup>#</sup>	Amended and Restated Executive Employment Agreement between Precision BioSciences, Inc. and Dr. Alan List, dated November 7, 2022.	10-K	001-38841	10.23	3/9/23	
10.21 <sup>#</sup>	Executive Employment Agreement, dated January 22, 2024, by and between Dario Scimeca and Precision BioSciences, Inc.	8-K	001-38841	10.3	1/23/2024	
10.22 <sup>#</sup>	Executive Employment Agreement, dated January 22, 2024, by and between Jeff Smith and Precision BioSciences, Inc.	8-K	001-38841	10.4	1/23/2024	
10.24 <sup>#</sup>	Form of Indemnification Agreement between Precision BioSciences, Inc. and its directors and officers.	S-1A	333-230034	10.17	3/18/2019	
10.25 <sup>#</sup>	Non Employee Director Compensation Plan (as amended).	10-Q	001-38841	10.1	5/9/2023	
10.26 <sup>#</sup>	Executive Employment Agreement, dated January 22, 2024, by and between Michael Amoroso and Precision BioSciences, Inc.	8-K	001-38841	10.1	1/23/2024	
21.1	Subsidiaries of Precision BioSciences, Inc.					*
23.1	Consent of Deloitte & Touche LLP.					*
31.1	Certification of Principal Executive Officer Pursuant to Rules 13a 14(a) and 15d 14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes Oxley Act of 2002.					*
31.2	Certification of Principal Financial Officer Pursuant to Rules 13a 14(a) and 15d 14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes Oxley Act of 2002.					*
32.1	Certification of Principal Executive Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes Oxley Act of 2002.					**
32.2	Certification of Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes Oxley Act of 2002.					**
97	Clawback policy					
101.INS	XBRL Instance Document					*
101.SCH	XBRL Taxonomy Extension Schema Document					*
104	Cover Page Interactive Data File (as formatted as Inline XBRL and contained in Exhibit 101)					*

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\* 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)(2)(ii) of Regulation S-K.

††† 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.



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## **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 balance sheets of Precision BioSciences, Inc. (the "Company") as of December 31, 2023 and 2022, the related statements of operations, changes in stockholders' equity, and cash flows, for each of the two years in the period ended December 31, 2023, 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, 2023 and 2022, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2023, 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 27, 2024

We have served as the Company's auditor since 2017.

**PART I. FINANCIAL INFORMATION**

**Item 1. Financial Statements.**

**PRECISION BIOSCIENCES, INC.**  
**BALANCE SHEETS**  
(In thousands, except share and per share amounts)

	<u>December 31, 2023</u>	<u>December 31, 2022</u>
<b>Assets</b>		
Current assets:		
Cash and cash equivalents	\$ 116,678	\$ 189,576
Accounts receivable	901	720
Prepaid expenses	5,977	6,025
Convertible note receivable	11,897	—
Other current assets	419	1,228
Assets held for sale	487	—
Current assets of discontinued operations	—	1,556
Total current assets	136,359	199,105
Property, equipment, and software—net	6,338	11,815
Intangible assets—net	400	731
Right-of-use assets—net	8,263	1,964
Investment in equity securities	3,206	2,576
Equity method investment	—	2,172
Note receivable—net	4,990	7,234
Other assets	225	226
Noncurrent assets of discontinued operations	—	12,346
Total assets	<u>\$ 159,781</u>	<u>\$ 238,169</u>
<b>Liabilities and Stockholders' Equity</b>		
Current liabilities:		
Accounts payable	\$ 2,968	\$ 653
Accrued compensation	4,978	5,104
Accrued research and development expenses	1,557	1,827
Deferred revenue	12,035	46,192
Lease liabilities	1,133	1,678
Loan payable—net	22,412	—
Other current liabilities	2,391	745
Current liabilities of discontinued operations	2,513	3,465
Total current liabilities	49,987	59,664
Deferred revenue	73,082	82,872
Lease liabilities	7,723	1,059
Long term debt—net	—	22,223
Other liabilities	—	201
Contract liabilities	10,000	10,000
Noncurrent liabilities of discontinued operations	128	1,717
Total liabilities	<u>140,920</u>	<u>177,736</u>
Commitments and contingencies (Note 13)		
Stockholders' equity:		
Preferred stock, \$0.0001 par value— 10,000,000 shares authorized as of December 31, 2023 and December 31, 2022; no shares issued and outstanding as of December 31, 2023 and December 31, 2022	—	—
Common stock; \$0.000005 par value— 200,000,000 shares authorized, 4,191,053 shares issued and 4,164,038 shares outstanding as of December 31, 2023; 3,725,689 shares issued and 3,698,674 shares outstanding as of December 31, 2022	1	1
Additional paid-in capital	509,443	489,696
Accumulated deficit	(489,631)	(428,312)
Treasury stock	(952)	(952)
Total stockholders' equity	18,861	60,433
Total liabilities and stockholders' equity	<u>\$ 159,781</u>	<u>\$ 238,169</u>

See notes to financial statements

**PRECISION BIOSCIENCES, INC.**  
**STATEMENTS OF OPERATIONS**  
(In thousands, except share and per share amounts)

	<b>For the Years Ended December 31,</b>	
	<b>2023</b>	<b>2022</b>
Revenue	\$ 48,727	\$ 25,098
Operating expenses		
Research and development	53,375	46,122
General and administrative	39,088	41,284
Total operating expenses	<u>92,463</u>	<u>87,406</u>
Operating Loss	(43,736)	(62,308)
Other income (expense), net:		
Impairment charges	—	(10,844)
Loss on disposal of assets	(461)	(30)
Gain (loss) on changes in fair value	1,145	(510)
Loss from equity method investment	(4,931)	(1,579)
Interest expense	(2,230)	(1,111)
Interest income	7,686	3,473
Total other income (expense), net	<u>1,209</u>	<u>(10,601)</u>
Loss from continuing operations	\$ (42,527)	\$ (72,909)
Loss from discontinued operations (including gain on disposal of \$8,446 during the year ended December 31, 2023)	(18,792)	(38,728)
Net loss	<u>\$ (61,319)</u>	<u>\$ (111,637)</u>
Net loss per share - basic and diluted	\$ (15.96)	\$ (38.10)
Weighted average shares of common stock outstanding- basic and diluted	3,841,405	2,929,873

See notes to financial statements



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

	Common Stock		Additional Paid-In Capital	Accumulated Deficit	Treasury Stock	Total Stockholders' Equity
	Shares	Amount				
<b>Balance- December 31, 2021</b>	2,057,085	—	\$ 408,795	\$ (316,675)	\$ (952)	\$ 91,168
Stock option exercises	11,186	—	392	—	—	392
Issuance of common stock under employee stock purchase plan	6,419	1	442	—	—	443
Share-based compensation expense	—	—	19,197	—	—	19,197
Restricted stock units vested	9,556	—	—	—	—	—
Issuance of common stock to collaboration partners	28,822	—	11,553	—	—	11,553
Net proceeds from issuance of common stock	1,612,621	—	49,317	—	—	49,317
Net loss	—	—	—	(111,637)	—	(111,637)
<b>Balance- December 31, 2022</b>	<u>3,725,689</u>	<u>\$ 1</u>	<u>\$ 489,696</u>	<u>\$ (428,312)</u>	<u>\$ (952)</u>	<u>\$ 60,433</u>
Stock option exercises	3,196	—	31	—	—	31
Issuance of common stock under employee stock purchase plan	18,101	—	370	—	—	370
Share-based compensation expense	—	—	14,040	—	—	14,040
Restricted stock units vested	46,893	—	—	—	—	—
Net proceeds from issuance of common stock	397,174	—	5,306	—	—	5,306
Net loss	—	—	—	(61,319)	—	(61,319)
<b>Balance- December 31, 2023</b>	<u>4,191,053</u>	<u>\$ 1</u>	<u>\$ 509,443</u>	<u>\$ (489,631)</u>	<u>\$ (952)</u>	<u>\$ 18,861</u>

See notes to financial statements

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

	<u>For the Years Ended December 31,</u>	
	<u>2023</u>	<u>2022</u>
<b>Cash flows from operating activities:</b>		
Net loss	\$ (61,319)	\$ (111,637)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	6,817	7,798
Share-based compensation	14,040	19,197
Loss on disposal of assets	563	106
Gain on disposal of business	(8,446)	—
Non-cash interest expense	368	295
Amortization of right-of-use assets	1,438	1,206
(Gain) Loss on changes in fair value	(1,145)	510
Loss from equity method investment	4,931	1,579
Amortization of discount on note receivable	(515)	(355)
Impairment charges	641	11,438
Changes in operating assets and liabilities:		
Prepaid expenses	1,051	(962)
Accounts receivable	(181)	(232)
Other assets and other current assets	1,752	1,431
Accounts payable	1,508	153
Other liabilities and other current liabilities	(724)	(1,816)
Deferred revenue	(43,947)	27,358
Lease liabilities	(946)	(1,822)
Contract liabilities	—	—
Net cash used in operating activities	<u>(84,114)</u>	<u>(45,753)</u>
<b>Cash flows from investing activities:</b>		
Proceeds from disposal of business	8,000	—
Proceeds from sale of equipment	107	—
Purchases of property, equipment and software	(1,957)	(3,319)
Purchases of intangibles assets	(321)	—
Net cash provided by (used in) investing activities	<u>5,829</u>	<u>(3,319)</u>
<b>Cash flows from financing activities:</b>		
Proceeds from stock option exercises	31	392
Proceeds from employee stock purchase plan	370	443
Proceeds from offering of common stock, net of issuance costs	4,986	49,345
Proceeds from offering of common stock to collaboration partners	—	25,000
Borrowings from revolving credit facility, net of issuance costs paid to lender	—	19,805
Net cash provided by financing activities	<u>5,387</u>	<u>94,985</u>
Net (decrease) increase in cash and cash equivalents	(72,898)	45,913
Cash and cash equivalents—beginning of period	189,576	143,663
Cash and cash equivalents—end of period	<u>\$ 116,678</u>	<u>\$ 189,576</u>
<b>Supplemental disclosures of noncash financing and investing activities:</b>		
Property, equipment and software additions included in accounts payable, accrued expenses and other current liabilities	<u>\$ 14</u>	<u>\$ 103</u>
Cash paid for interest	<u>\$ 2,018</u>	<u>\$ 824</u>
Unsettled at-the-market issuances of common stock included in other current assets	<u>\$ 320</u>	<u>\$ —</u>

See notes to financial statements

**Precision BioSciences, Inc.**  
**Notes to 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 gene editing company dedicated to improving life by developing *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, 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 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 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 financial statements and disclosures made in the accompanying notes to the 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.

**Basis of Presentation**

These financial statements have been prepared in accordance with GAAP. Additionally, the accompanying 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.

The accompanying financial statements have been recast for all periods presented to reflect the assets, liabilities and expenses related to discontinued operations (discussed below). The accompanying financial statements are generally presented in conformity with the Company’s historical format.

**Reverse Stock Split**

On February 13, 2024, the Company amended its amended and restated certificate of incorporation in order to effect a 1-for-30 reverse stock split of its outstanding shares of capital stock (the “Reverse Stock Split”). As a result of the Reverse Stock Split, every 30 shares of the Company’s common stock issued or outstanding were automatically reclassified into one new share of common stock, subject to the treatment of fractional shares as described below, without any action on the part of the holders. All historical share and per-share amounts reflected throughout the accompanying consolidated financial statements and other financial information in this Annual Report on Form 10-K have been retroactively adjusted to reflect the 2024 Reverse Stock Split as if the split occurred as of the earliest period presented. The Reverse Stock Split did not affect the number of authorized shares of common stock or the par value of the common stock. No fractional shares were issued in connection with the Reverse Stock Split. Stockholders who would otherwise have been entitled to receive fractional shares as a result of the Reverse Stock Split were entitled to a cash payment in lieu thereof at a price equal to the fraction to which the stockholder would otherwise be entitled multiplied by the closing sales price per share of the common stock (as adjusted to give effect to the Reverse Stock Split) on The Nasdaq Capital Market on February 13, 2024, the last trading day immediately preceding the effective time of the Reverse Stock Split.

**Summary of Significant Accounting Policies**

**Cash and Cash Equivalents**

As of December 31, 2023, the Company held cash equivalents which are composed of money market funds. As of December 31, 2022, the Company held cash equivalents which were composed of money market funds and repurchase agreements that were purchased through repurchase intermediary banks and collateralized by deposits in the form of government securities and obligations.

### **Concentrations of Credit Risk**

Financial instruments that potentially subject the Company to concentrations of credit risk consist principally of cash, cash equivalents, 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 Prevail and Novartis accounted for 53% and 47% of revenue during the year ended December 31, 2023, respectively. Revenue from Prevail and Novartis accounted for 62% and 38% of revenue during the year ended December 31, 2022, respectively. Prevail and Novartis accounted for 62% and 38% of deferred revenue as of December 31, 2023, respectively.

In addition, the Company currently holds a \$10.0 million promissory note payable from Elo (defined below) and a \$13.0 million convertible note from Imugene US (defined below), which exposes the Company to potential losses in the event of default. Counterparty credit risk is monitored through periodic reviews of financial records. As of December 31, 2023, 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 in-licenses and capitalized patent costs. 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 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 data, 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 balance sheets and records changes in fair value in the statements of operations as a component of other income or expense.

As of December 31, 2023 and December 31, 2022 the Company held common stock in iECURE (defined below) with a fair value of \$3.2 million and \$2.6 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.



## 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, 2023, the Company recorded cumulative catch up adjustments on its contracts with partners that increased revenue recognition by \$1.6 million; the cumulative catch-up adjustments resulted from a change in total estimated effort required to satisfy performance obligations and changes in variable consideration included in the transaction price related to estimated fees to be received from partners. During the year ended December 31, 2023, the Company recorded \$48.7 million in revenue that was included in deferred revenue as of December 31, 2022.

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 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 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 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.

## **Discontinued Operations**

The Company determined that its decision to no longer internally develop *ex vivo* allogeneic chimeric antigen receptor (“CAR T”) immunotherapies and related sale of our CAR T infrastructure to Imugene (defined below) met the criteria for classification as a discontinued operation in accordance with ASC Subtopic 205-20, *Discontinued Operations*. Accordingly, the accompanying financial statements for all periods have been updated to present the assets and liabilities associated with the development of *ex vivo* allogeneic CAR T immunotherapies separately as discontinued operations on the balance sheets and the results of all discontinued operations are reported as a separate component in the statements of operations.

For additional information related to discontinued operations, refer to Note 6, *Discontinued Operations*.

## **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, 2023 and December 31, 2022, there was no difference between net loss and comprehensive loss in the accompanying statements 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, 2023 and December 31, 2022, 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 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 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**

Accounting standards updates issued, but not effective until after December 31, 2023, are not expected to have a material effect on the Company's financial position, statements of operations or cash flows.

## **NOTE 2: COLLABORATION AND LICENSE AGREEMENTS**

### **TG Therapeutics**

On January 7, 2024, the Company entered into a license agreement (the “TG License Agreement”) with TG Cell Therapy, Inc. (“TG Subsidiary”) and its parent company TG Therapeutics, Inc. (“TG Parent” and, together with TG Subsidiary, “TG Therapeutics”), pursuant to which the Company granted TG Subsidiary certain exclusive and non-exclusive license rights to develop, manufacture, and commercialize the Company’s allogeneic CAR T therapy azer-cel for autoimmune diseases and other indications outside of cancer (collectively referred to as licensed products).

Under the TG License Agreement, the Company is entitled to receive an upfront cash payment of \$10.0 million (the “TG Upfront Payment”), an additional cash payment of \$7.5 million in the event that TG Therapeutics achieves a certain clinical milestone that is expected to be achieved in the near-term (the “Initial Milestone Payment”), and additional payments upon the achievement of additional specified milestones of up to \$288.6 million (the “Additional TG Milestone Payments”). As described below, up to \$10.0 million of the cash payments potentially payable to the Company are payable in exchange for the issuance to TG Subsidiary by the Company of shares of the Company’s common stock (the “Company Stock Issuances”).

The TG Upfront Payment of \$10.0 million is comprised of (i) a \$5.25 million cash payment that was paid to the Company on February 5, 2024, (ii) a \$2.25 million cash payment that was paid to the Company on February 4, 2024, in exchange for 97,360 shares of the Company’s common stock, based on a price per share equal to 200% of the volume-weighted-average-price (“VWAP”) of the Company’s common stock for the 30 trading days prior to the date of the TG License Agreement, and (iii) a deferred cash payment of \$2.5 million due within 12 months following the date of the TG License Agreement, payable in exchange for such number of shares of the Company’s common stock determined based on a price per share equal to the greater of (A) 200% of the VWAP of the Company’s common stock for the 30 trading days prior to the date of payment or (B) a minimum price of \$11.1660 determined in accordance with Nasdaq Listing Rule 5635(d) (the “Minimum Price”).

The Initial Milestone Payment of \$7.5 million, if payable, will consist of (i) a \$5.25 million cash milestone payment and (ii) a \$2.25 million cash payment payable in exchange for such number of shares of the Company’s common stock determined based on a price per share equal to the greater of (A) 200% of the VWAP of the Company’s common stock for the 30 trading days prior to the achievement of such milestone or (B) the Minimum Price.

The Additional TG Milestone Payments become due upon the achievement of certain milestones as specified in the TG License Agreement. Included within the Additional TG Milestone Payments is a potential payment of \$3.0 million in connection with achievement of a milestone specified in the TG License Agreement, payable in exchange for such number of shares of the Company’s common stock determined based on a price per share equal to the greater of (A) 200% of the VWAP of the Company’s common stock for the 30 trading days prior to the achievement of such milestone or (B) the Minimum Price.

Subject to the terms and conditions of the TG License Agreement, TG Therapeutics is permitted to pay up to 50% of the value of each Additional Milestone Payment (other than the Additional Milestone Payment described above that would, upon achievement, involve the issuance of \$3.0 million of Shares by Precision) in freely tradable shares of common stock of TG Parent, valued based on the VWAP of the TG Parent shares of common stock on Nasdaq for the 30 trading days prior to the achievement of the applicable milestone.

If a licensed product under the TG License Agreement is approved and sold, TG Therapeutics is also required to pay the Company tiered royalties ranging from high-single-digit to low-double-digit percentages on net sales of the licensed product. TG Therapeutics’ 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 (i) the expiration of the last-to-expire valid claim in such country covering such licensed product; (ii) the expiration of any period of data, regulatory, or market exclusivity, or supplemental protection certificates (other than patents) covering the licensed product in such country; and (iii) a period of ten years following the first commercial sale of the respective licensed product in such country.

Unless earlier terminated, the TG License Agreement will remain in effect on a licensed product-by-licensed product and country-by-country basis until the expiration of a defined royalty term for each licensed product and country. The Company may terminate the TG License Agreement if TG Therapeutics fails to initiate certain development activities with respect to the licensed product by a specified date or ceases active development of the licensed product for a specified period of time. In addition, the Company may terminate the TG License Agreement if TG Therapeutics or any of its affiliates or sublicensees challenges the validity of any patents controlled by the Company. Each of the Company and TG Therapeutics may terminate the TG License Agreement (i) for material breach by the other party and a failure to cure such breach within the time period specified in the TG License Agreement or (ii) the other party’s insolvency.

#### **Sale of Azer-cel CAR T Platform to Imugene**



On August 15, 2023, the Company entered into an asset purchase agreement (the “Imugene Purchase Agreement”) with Imugene Limited, and its wholly-owned subsidiary Imugene (USA) Inc. (“Imugene US” and together with Imugene Limited, “Imugene”). Pursuant to and simultaneously with the execution of the Imugene Purchase Agreement, on August 15, 2023 (the “Closing Date”), Imugene US acquired the Company’s manufacturing infrastructure used in the development and manufacture of azer-cel, including assuming the lease to the Company’s manufacturing facility and certain contracts of the Company with respect to the Company’s manufacturing facility, and related equipment, supplies, azer-cel clinical trial inventory and other assets related to the Company’s CAR T cell therapy platform. As part of the Imugene Purchase Agreement, Imugene US hired a number of employees of the Company who were associated with the Company’s historical CAR T cell therapy operations.

In consideration for the assets acquired under the Imugene Purchase Agreement, Imugene US assumed certain liabilities of the Company, paid the Company \$8 million in cash, and issued to the Company convertible notes pursuant to the terms and conditions set forth in a convertible note subscription deed (collectively, the “Imugene Convertible Note”) in an aggregate principal amount of \$13 million. The Imugene Convertible Note is non-interest bearing and matures on the first anniversary of the Closing Date (the “Maturity Date”). On the Maturity Date, the Imugene Convertible Note will be redeemed with cash, converted into ordinary shares of Imugene Limited at a conversion price based on the 10-day volume weighted average price of Imugene Limited’s ordinary shares prior to the date of conversion, or partially redeemed with cash and partially converted into shares, at Imugene's discretion.

Additionally, the Company and Imugene US entered into a license agreement (the “Imugene License Agreement”) on the Closing Date, pursuant to which the Company granted Imugene US certain exclusive and non-exclusive license rights to develop, manufacture, and commercialize oncological applications of the Company’s allogeneic CAR T therapy, azer-cel, and up to three additional research product candidates directed to targets that Imugene US may nominate prior to the fifth anniversary of the effective date of the Imugene License Agreement, pursuant to the terms of the Imugene License Agreement.

In addition, under the Imugene License Agreement, the Company is eligible to receive milestone payments of up to an aggregate of \$206 million for azer-cel, inclusive of a payment of \$8 million in cash and equity upon successful completion of the Phase 1b dosing in the CAR T relapsed large B cell lymphoma (“LBCL”) patient population. For azer-cel, the Company is eligible to receive double-digit royalties on net sales. For up to three additional research programs to be developed by Imugene, the Company is eligible for up to \$145 million in milestone payments and, if licensed products are approved and sold, tiered royalties ranging from the mid-single digit to low-double digit percentages on net sales of such licensed products. In addition, the Company is eligible to receive mid-single digit percentage-based fees for certain change of control transactions involving Imugene and for partnering transactions involving a licensed product. Imugene’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 the first commercial sale of the respective licensed product.

Unless earlier terminated, the Imugene License Agreement will remain in effect on a licensed product-by-licensed product and country-by-country basis until the expiration of a defined royalty term for each licensed product and country. The Company may terminate the entire Imugene License Agreement due to a challenge to its patents brought by Imugene and a breach by Imugene in any material respect of the Imugene License Agreement, the Imugene Purchase Agreement or any related transaction documents. The Company may also terminate the Imugene License Agreement with respect to azer-cel if Imugene fails to initiate certain development activities with respect to azer-cel by a specified date, if Imugene fails to expend certain amounts on the development of azer-cel or if Imugene ceases active development of azer-cel for a specified period of time. Either party may terminate the License Agreement (i) for material breach by the other party and a failure to cure such breach within the time period specified in the agreement or (ii) the other party’s insolvency.

The Company assessed the Imugene License Agreement in accordance with ASC 606 and concluded that the promises in the Imugene License represent a transaction with a customer. The Company has concluded that the Imugene License Agreement contains the following promises: (i) the license to develop, manufacture, and commercialize oncological applications of the azer-cel and up to three additional research product candidates and (ii) JSC (“Joint Steering Committee”) Participation. 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. Accordingly, the Company concluded that the promise of the license is a single performance obligation.

The Company concluded the Imugene License Agreement represents functional intellectual property in accordance with ASC 606 given the Company will not be providing any additional services to Imugene outside of the right to use the licensed intellectual property. As of December 31, 2023, management has constrained all variable consideration related to milestone payments in the Imugene License given the level of uncertainty associated with achievement of the milestone payments. Accordingly, no revenue was recognized under the Imugene License Agreement during the year ended December 31, 2023.



## 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 (collectively referred to as licensed products). Any initial licensed products under the Novartis Agreement 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 413,581 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 \$60.30 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 years ended December 31, 2023 and 2022, the Company recognized revenue under the Novartis Agreement of \$22.7 million and \$9.5 million, respectively. Deferred revenue related to the Novartis Agreement amounted to \$32.4 million and \$54.2 million as of December 31, 2023 and December 31, 2022, respectively, of which \$7.4 million and \$27.9 million, respectively, was included in current liabilities within the balance sheets.

### **Development and License Agreement with Prevail**

On November 19, 2020, the Company entered into a development and license 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, which was subsequently assigned to Prevail Therapeutics Inc., a wholly-owned subsidiary of Eli Lilly and Company (“Prevail”), effective November 1, 2022 (the “Original Prevail Agreement”).

On June 30, 2023, the Company entered into an amended and restated development and license agreement (the “Prevail Agreement”) with Prevail. The Prevail Agreement amends and restates the Original Prevail Agreement. Pursuant to the terms of the Prevail Agreement, Prevail and the Company will continue to collaborate on developing the Company’s ARCUS nucleases for the research and development of potential *in vivo* therapies for genetic disorders, including Duchenne muscular dystrophy, a liver-directed target, and a central nervous system directed target. Prevail also continues to have the right to nominate up to three additional gene targets for genetic disorders over the initial nomination period of four years. Prevail may extend the nomination period for an additional two years from the date on which such initial nomination period ends, upon Prevail’s election and payment of an extension fee. Additionally, Prevail has the option to replace up to two gene targets upon Prevail’s election and payment of a replacement target fee.

The Company will continue to oversee creation, selection, *in vitro* development, and optimization of ARCUS nucleases with respect to the gene targets subject to the collaboration. Prevail will oversee and fund preclinical research and IND-enabling activities which were previously to be conducted by the Company at the Company’s expense. Manufacturing initial clinical trial material for the first licensed product, which was previously the Company’s responsibility to conduct at Prevail’s expense, will instead be Prevail’s responsibility at Prevail’s expense. Prevail will continue to 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.

In connection with the closing of the Original Prevail Agreement on January 6, 2021, the Company received an upfront cash payment of \$100.0 million. Under the Prevail Agreement, the Company will also be eligible to receive milestone payments of up to an aggregate of \$390 million to \$395 million per licensed product, a decrease from \$420 million as provided in the Original Prevail Agreement, as well as nomination fees for additional and replacement targets and certain research funding. The terms of potential nomination fees for additional targets and royalties on worldwide net sales of licensed products for which the Company may become eligible, as well as the

terms of the Company's right to elect to co-fund the clinical development of one licensed product under the Original Prevail Agreement, are not modified by the terms of the Prevail Agreement. 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. Prevail'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 Original Prevail Agreement, the Company and Lilly entered into a Share Purchase Agreement (the "Lilly Share Purchase Agreement"), pursuant to which Lilly purchased 125,406 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 Original Prevail 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 Prevail contains the following promises: (i) license of intellectual property; (ii) performance of R&D services, (iii) JSC Participation, and (iv) regulatory responsibilities. The Company determined that the license of intellectual property, R&D services, and regulatory responsibilities were not distinct from each other, as the license, R&D services, 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, 2023 and 2022, the Company recognized revenue under the Prevail Agreement of \$26.0 million and \$15.6 million, respectively. Deferred revenue related to the Prevail Agreement amounted to \$52.7 million and \$74.8 million as of December 31, 2023 and December 31, 2022, respectively, of which \$4.7 million and \$18.3 million, respectively, was included in current liabilities within the balance sheets.

### **Development and License Agreement with iECURE**

In August 2021, the Company entered into a development and license agreement with iECURE (the "iECURE DLA") under which iECURE was to advance the Company's PBGENE-PCSK9 candidate through preclinical activities as well as a 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 "PCSK9 License"), including ornithine transcarbamylase ("OTC") deficiency, Citrullinemia Type 1 ("CTLN1"), Phenylketonuria, and another program focused on liver disease. Simultaneously with the entry into the iECURE DLA, the Company and iECURE entered into an Equity Issuance Agreement (the "iECURE Equity 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 Agreement was to be combined with the iECURE DLA (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 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, 2023, the Company recorded a \$0.6 million increase in the carrying value of its iECURE equity to adjust to fair value as iECURE has progressed towards a clinical trial for OTC deficiency. 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 issued 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 recorded to the prepaid expenses and other assets line items of the Company's 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 a Phase 1 clinical trial. During the year ended December 31, 2022, the Company recognized \$2.1 million of research and development expense related to amortization of the PCSK9 Prepaid. 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 familial hypercholesterolemia with iECURE as its partner in December 2022. Accordingly, there was no PCSK9 Prepaid balance as of December 31, 2023 or December 31, 2022.

**NOTE 3: SHARE-BASED COMPENSATION**

The Company previously granted stock options under its 2015 Stock Incentive Plan (the “2015 Plan”). As of December 31, 2023 there were 36,552 stock options outstanding under the 2015 Plan and no remaining stock options available to be granted under the 2015 Plan.

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 211,303 stock options and 214,857 restricted stock units (“RSUs”) outstanding as of December 31, 2023.

The number of shares available for issuance under the 2019 Plan initially equaled 158,333 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, 2023, the aggregate number of shares available for issuance under the 2019 Plan has been increased by 367,616 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, 2023, 122,630 shares were available to be issued under the 2019 Plan.

Up to 17,500 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, 2023, the aggregate number of shares available for issuance under the 2019 ESPP has been increased by 91,903 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, 2023, we had issued 33,080 shares under the 2019 ESPP. As of December 31, 2023, 76,323 shares were available to be issued under the 2019 ESPP. The Company recognized share-based compensation expense related to the ESPP of \$0.1 million and \$0.2 million during the years ended December 31, 2023 and 2022, 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 300,000 shares of the Company’s common stock may be issued under the Inducement Award Plan. As of December 31, 2023, 190,739 shares were available to be issued under the Inducement Award Plan. The Inducement Award Plan had 101,807 stock options and no RSUs outstanding as of December 31, 2023.

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

	<b>Years Ended December 31,</b>	
	<b>2023</b>	<b>2022</b>
Employee	\$ 12,364	\$ 15,921
Nonemployee	1,676	3,276
	<u>\$ 14,040</u>	<u>\$ 19,197</u>



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

	Years Ended December 31,	
	2023	2022
Research and development	\$ 4,355	\$ 7,973
General and administrative	9,685	11,224
	<u>\$ 14,040</u>	<u>\$ 19,197</u>

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,	
	2023	2022
Estimated dividend yield	0.00%	0.00%
Weighted-average expected stock price volatility	87.15%	79.66%
Weighted-average risk-free interest rate	3.89%	2.57%
Expected term of options (in years)	5.78	6.07
Weighted-average fair value per option	\$ 17.41	\$ 55.91

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, 2022 and December 31, 2023 :

	Outstanding Option Shares	Weighted- Average Exercise Price
Balance as of December 31, 2021	330,386	278.33
Granted	223,670	80.71
Exercised	(11,186)	35.13
Forfeited/canceled	(85,773)	259.72
Balance as of December 31, 2022	457,097	191.07
Granted	20,443	23.61
Exercised	(3,196)	9.59
Forfeited/canceled	(124,682)	221.38
Balance as of December 31, 2023	<u>349,662</u>	<u>172.13</u>

The intrinsic value of stock options exercised was less than \$0.1 million and \$0.7 million during the years ended December 31, 2023 and December 31, 2022, respectively.

During the year ended December 31, 2023, the Company granted 161,161 RSUs with a grant date fair value of \$5.6 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, 2022 and December 31, 2023:

	RSU Awards	Weighted-Average Grant Date Fair Value
Unvested RSUs as of December 31, 2021	25,668	338.76
Granted	110,842	78.73
Forfeited	(6,404)	214.04
Vested	(9,556)	336.29
Unvested RSUs as of December 31, 2022	120,550	106.49
Granted	161,161	34.49
Forfeited	(19,961)	109.19
Vested	(46,893)	112.02
Unvested RSUs As of December 31, 2023	214,857	51.03

There was approximately \$16.7 million of total unrecognized compensation cost related to unvested stock options and RSUs as of December 31, 2023, which is expected to be recognized over a weighted-average period of 1.8 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, 2023 and December 31, 2022.

Years Ended December 31,		Number of Options	Weighted- Average Remaining Contractual Life (in years)	Weighted- Average Exercise Price
2023	Expected to be exercisable	349,662	7.15	\$ 172.13
2023	Currently exercisable	223,019	6.58	\$ 199.00
2022	Expected to be exercisable	457,097	6.59	\$ 191.07
2022	Currently exercisable	176,113	4.56	\$ 275.62

The following table summarizes certain information about stock options outstanding under the stock option plans for the years ended December 31, 2023 and December 31, 2022, respectively:

Year Ended December 31, 2023			
Exercise price	Number of Options Outstanding	Weighted- Average Remaining Life	Number of Options Exercisable
\$12.30 - \$46.50	67,401	7.65	27,084
\$50.40 - \$100.20	77,327	8.34	49,906
\$122.40 - \$174.90	64,477	7.35	35,163
\$189.30 - \$293.70	65,372	7.10	46,526
\$305.10 - \$480.00	75,085	5.33	64,340
	349,662		223,019

Year Ended December 31, 2022			
Exercise price	Number of Options Outstanding	Weighted- Average Remaining Life	Number of Options Exercisable
\$0.60 - \$46.50	67,565	7.03	20,547
\$50.40 - \$100.20	81,367	9.14	194
\$122.40 - \$136.80	73,906	7.13	47
\$170.10 - \$293.70	117,590	5.85	69,761
\$305.10 - \$480.00	116,669	4.96	85,564
	457,097		176,113

#### NOTE 4: RETIREMENT PLAN

In January 2011, the Company established a defined contribution 401(k) retirement savings plan (the "Retirement Plan") available 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, 2023 and December 31, 2022.

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 to the Retirement Plan during each of the years ended December 31, 2023 and December 31, 2022, 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 statements of operations.

**NOTE 5: IMPAIRMENT CHARGES**

The Company did not record any impairment charges in continuing operations during the year ended December 31, 2023. During the year 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 represented the remaining unamortized balance of the PCSK9 Prepaid.

**NOTE 6: DISCONTINUED OPERATIONS**

The Company determined that the sale of its cell therapy operations qualified for discontinued operations accounting treatment in accordance with ASC 205-20.

The historical balance sheet and statements of operations of the Company and the related notes to the financial statements have been presented as discontinued operations in the financial statements and prior periods have been recast. Discontinued operations include the results of the Company's historical cell therapy operations.

The following table shows amounts included in assets and liabilities of discontinued operations, respectively, on the Company's balance sheets as of December 31, 2023 and December 31, 2022:

	<u>December 31, 2023</u>	<u>December 31, 2022</u>
<b>Current assets of discontinued operations</b>		
Prepaid expenses	—	1,527
Assets held for sale	—	—
Other current assets	—	29
Total current assets of discontinued operations	—	1,556
<b>Noncurrent assets of discontinued operations</b>		
Property, equipment, and software—net	—	8,375
Intangible assets—net	—	617
Right-of-use assets—net	—	1,010
Other assets	—	2,344
Total noncurrent assets of discontinued operations	—	12,346
Total assets of discontinued operations	<u>—</u>	<u>13,902</u>
<b>Current liabilities of discontinued operations</b>		
Accounts payable	158	572
Accrued compensation	—	1,155
Accrued research and development expenses	2,355	1,379
Lease liabilities	—	359
Total current liabilities of discontinued operations	2,513	3,465
<b>Noncurrent liabilities of discontinued operations</b>		
Lease liabilities	—	1,717
Total noncurrent liabilities of discontinued operations	—	1,717
Total liabilities of discontinued operations	<u>2,513</u>	<u>5,182</u>

The following table summarizes the results of operations of the Company's discontinued operations for the years ended December 31, 2023 and 2022:

	For the Years Ended December 31,	
	2023	2022
Classes of expenses constituting loss from discontinued operations		
Research and development expense	(26,438)	(37,817)
General and administrative expense	(57)	(241)
Impairment of long lived assets	(641)	(594)
Loss on disposal of assets	(102)	(76)
Loss from discontinued operations related to classes of expenses	(27,238)	(38,728)
Gain from disposal of discontinued operations	8,446	—
Income tax benefit from discontinued operations	—	—
Loss from discontinued operations	(18,792)	(38,728)

The following table presents the significant non-cash items and proceeds from sales of assets related to discontinued operations for the years ended December 31, 2023 and 2022 that are included in the accompanying statements of cash flows:

	For the Years Ended December 31,	
	2023	2022
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	1,631	2,582
Share-based compensation	713	2,563
Impairment charges	641	594
Loss on disposal of assets	102	76
Gain on disposal of business	(8,446)	—
Cash flows provided by investing activities		
Proceeds from disposal of business	8,000	—
Proceeds from sale of equipment	37	—

#### NOTE 7: 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,	
	2023	2022
Loss from continuing operations (in thousands)	\$ (42,527)	\$ (72,909)
Loss from discontinued operations (in thousands)	\$ (18,792)	\$ (38,728)
Net loss (in thousands)	<u>\$ (61,319)</u>	<u>\$ (111,637)</u>
Weighted-average common shares outstanding basic and diluted	3,841,405	2,929,873
Loss per share basic and diluted:		
Loss from continuing operations	(11.07)	(24.88)
Loss from discontinued operations	(4.89)	(13.22)
Net loss per share, basic and diluted	<u>(15.96)</u>	<u>(38.10)</u>

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,	
	2023	2022
Unvested restricted stock units	230,646	73,300
Stock Options	10,345	79,222
Unsettled ESPP contributions	8,065	2,044
Total common stock equivalents excluded from diluted net loss per share	<u>249,056</u>	<u>154,566</u>

**NOTE 8: PROPERTY, EQUIPMENT AND SOFTWARE AND ASSETS HELD FOR SALE**

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

	2023	2022
Construction in progress	\$ 70	\$ 520
Leasehold improvements	11,945	11,946
Software	432	442
Laboratory equipment	15,856	17,271
Office equipment	1,399	1,408
Furniture and fixtures	2,124	2,097
Total property, equipment and software	31,826	33,684
Less accumulated depreciation and amortization	25,488	21,869
Property, equipment and software - net	\$ 6,338	\$ 11,815

Depreciation expense for continuing operations, including amortization of leasehold improvements and software, was \$5.2 million for the years ended December 31, 2023 and 2022.

As of December 31, 2023, the Company had \$0.5 million in property, plant, and equipment that met the criteria for classification as held for sale. These assets are recognized at the lower of net book value or fair value less costs to sell using a market approach. The Company evaluated the fair value of its assets held for sale and determined fair value of the assets held for sale less costs to sell exceeded net book value. Accordingly, the Company recorded an impairment of \$0.5 million on assets held for sale during the year ended December 31, 2023 to reflect the difference between net book value and the fair value less costs to sell of assets held for sale. The related impairment is recognized in the accompanying statement of operations in the loss on disposal of assets line item.

**NOTE 9: INTANGIBLE ASSETS**

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

	2023	2022
License cost	\$ 548	\$ 910
Less: accumulated amortization	(148)	(179)
Intangible assets, net	\$ 400	\$ 731

Amortization expense of intangible assets was less than \$0.1 million and \$0.1 million for the years ended December 31, 2023 and December 31, 2022, 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 \$0.2 million amortized to expense in 2029 and beyond.

**NOTE 10: FAIR VALUE MEASUREMENTS**

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

December 31, 2023	Fair Value	Level 1	Level 2	Level 3
<b>Assets:</b>				
Money market funds	\$ 13,960	\$ 13,960	\$ —	\$ —
Investment in iECURE	3,206	—	—	3,206
Imugene convertible note	11,897	—	11,897	—
Assets held for sale	487	—	—	487
	<u>\$ 29,550</u>	<u>\$ 13,960</u>	<u>\$ 11,897</u>	<u>\$ 3,693</u>
<b>Liabilities:</b>				
Final payment fee	\$ 215	\$ —	\$ 215	\$ —
	<u>\$ 215</u>	<u>\$ —</u>	<u>\$ 215</u>	<u>\$ —</u>

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
	<u>\$ 43,444</u>	<u>\$ 868</u>	<u>\$ 40,000</u>	<u>\$ 2,576</u>
Liabilities:				
Final payment fee	\$ 199	\$ —	\$ 199	\$ —
	<u>\$ 199</u>	<u>\$ —</u>	<u>\$ 199</u>	<u>\$ —</u>

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, 2023 (in thousands):

	Investment in iECURE
Balance December 31, 2022	\$ 2,576
Additions	—
Gains from changes in fair value included in earnings	630
Balance December 31, 2023	<u>\$ 3,206</u>

The carrying amounts of the Company's financial instruments, including accounts receivable, accounts payable, and accrued expenses and other current liabilities, approximate their respective fair values due to their short-term nature. The Company uses a three-tier fair value hierarchy to classify and disclose all assets and liabilities measured at fair value on a recurring basis and to minimize the use of unobservable inputs when determining their fair value. The three tiers are defined as follows:

Level 1—Observable inputs based on unadjusted quoted prices in active markets for identical assets or liabilities

Level 2—Inputs, other than quoted prices in active markets, that are observable either directly or indirectly

Level 3—Unobservable inputs for which there is little or no market data, which require the Company to develop its own assumptions

### Cash Equivalents

As of December 31, 2023, the Company held cash equivalents which are composed of money market funds. As of December 31, 2022, the Company held cash equivalents which were composed of money market funds and repurchase agreements that were purchased through repurchase intermediary banks and collateralized by deposits in the form of government securities and obligations. The 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, 2023, the Company recorded a \$0.6 million increase in the carrying value of its iECURE equity to adjust to fair value.

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

### Assets Held for Sale

The fair values of property, plant, and equipment held for sale is classified as Level 3 in the fair value hierarchy due to a mix of unobservable inputs utilized such as independent research in the market as well as actual quotes from market participants.

### Imugene Convertible Note



As partial consideration for the assets acquired by Imugene in connection with the Purchase Agreement, Imugene US issued to the Company the Imugene Convertible Note in an aggregate principal amount of \$13 million. The Imugene Convertible Note is non-interest bearing and matures on August 15, 2024. On the Maturity Date, the Imugene Convertible Note must be redeemed with cash, converted into ordinary shares of Imugene Limited at a conversion price based on the 10-day volume weighted average price of Imugene Limited's ordinary shares prior to the date of conversion, or partially redeemed with cash and partially converted into shares, at Imugene's discretion.

The Company classifies the Imugene Convertible Note within Level 2 of the fair value hierarchy as the assessed fair value is based on observable market inputs including the risk-free rate and the ordinary share price, volume, and volatility.

### **Final Payment Fee**

The Company is required to pay a final payment fee upon maturity of the Revolving Line (as defined in Note 12, *Debt*, below). 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). There was an assessed loss on change in fair value of the final payment fee of less than \$0.1 million during the year ended December 31, 2023.

The Company classifies the final payment fee within Level 2 of the fair value hierarchy as the assessed fair value is based on observable market inputs including the Company's current borrowing rate. The final payment fee is included in other current liabilities within the balance sheet as of December 31, 2023 and other noncurrent liabilities within the balance sheet as of December 31, 2022.

### **NOTE 11: ELO TRANSACTION**

On December 17, 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 ("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. As consideration for the assets contributed and license granted by the Company to Elo, the Company received Common Stock in Elo and a \$10.0 million promissory note payable from Elo (the "Note Receivable").

### **Investment in Elo**

It was determined that the Company possesses the ability to exercise significant influence over the operating and financial policies of Elo. Accordingly, the Company accounts for its investment in Elo under the equity method.

The Company owned approximately 37% of Elo's voting shares outstanding as of December 31, 2023 and 2022. The Company's proportionate share of Elo's net loss for the years ended December 31, 2023 and 2022 was \$4.9 million and \$6.3 million, respectively. As the Company's cumulative proportionate share of Elo's net loss exceeded the carrying value of the investment in Elo, the carrying value of the Investment in Elo has been reduced to \$0. In accordance with ASC 323, the Company will continue to record its proportionate share of Elo's net loss in the statements of operations along with a corresponding reduction in the carrying value of the Note Receivable.

### **Note Receivable**

The Note Receivable matures on the earlier of (i) December 1, 2028 or (ii) a Deemed Liquidation Event (as defined in the Elo's Amended and Restated Certificate of Incorporation). The Note Receivable accrues interest at 2.00% per annum and is payable annually on December 17th.

As of December 31, 2023, the carrying value of the Note Receivable was \$5.0 million including a \$2.8 million decrease in the carrying value as a result of equity method investment losses. The remaining \$5.0 million discount on the Note Receivable will be amortized to interest income over the life of the Note.

**NOTE 12: DEBT**

Pursuant to the terms of the loan and security agreement with Pacific Western Bank (“PWB”) the Company may request advances on a revolving line of credit of up to an aggregate principal amount of \$30.0 million (as amended from time to time, the “Revolving Line”) at an interest rate equal to the greater of (a) 0.75% above the Prime rate (as defined in the Revolving Line) and (b) 4.25%. As of December 31, 2023, the stated interest rate on the Revolving Line was 9.25% and the effective interest rate was 10.3%.

The Revolving Line maturity date is June 23, 2024 and all outstanding principal amounts are due upon maturity. 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.

As of December 31, 2023 and December 31, 2022, \$22.5 million in borrowings were outstanding under the Revolving Line and the unamortized debt discount balance was less than \$0.1 million and \$0.3 million, respectively.

## **NOTE 13: 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 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. 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 financial statements.

Accordingly, contingent liabilities of \$10.0 million related to the Program Purchase Agreement are accrued and included in contract liabilities in the balance sheets as of December 31, 2023 and December 31, 2022.

### **Leases**

The Company has an operating lease for real estate in North Carolina and does not have any finance leases.

On October 16, 2023, the Company and Venable Historic, LLC, successor-in-interest to Venable Tenant, LLC (the “Landlord”), entered into a Tenth Amendment to Lease Agreement (the “Lease Amendment”), which amended certain terms of the Lease Agreement dated April 5, 2010, as amended (the “Original Lease”) with respect to the Company’s headquarters facilities located in Durham, North Carolina. Among other things, the Lease Amendment extends the term of the Original Lease for an additional period of five years commencing upon August 1, 2024 and up to and through July 31, 2029.

The Company has existing leases in which the non-lease components (e.g., common area maintenance, consumables, etc.) are paid separately from rent based on actual costs incurred and therefore are not included in the right-of-use assets and lease liabilities but rather reflected as an expense in the period incurred.

The elements of lease expense were as follows:

(in thousands)	For the Years Ended December 31,	
	2023	2022
<b>Lease Cost</b>		
Operating lease cost	\$ 2,043	\$ 1,644
Short-term lease cost	742	563
Variable lease cost	692	746
Sublease income	(137)	—
<b>Total Lease Cost</b>	<b>\$ 3,340</b>	<b>\$ 2,953</b>
<b>Other Information</b>		
Operating cash flows used for operating leases	2,026	2,264
Operating right-of-use assets obtained in exchange for lease obligations	9,955	—
Operating lease liabilities arising from obtaining right-of-use assets	9,328	—
<b>Operating Leases</b>		
Weighted average remaining lease term (in years)	5.6	2.9
<b>Operating Leases</b>		
Weighted average discount rate	9.2%	7.7%

Future lease payments under non-cancelable operating leases with terms of greater than one year as of December 31, 2023, were as follows:

(in thousands)	December 31, 2023
2024	\$ 1,888
2025	1,962
2026	2,019
2027	2,078
2028	2,140
2029 and beyond	1,269
<b>Total lease payments</b>	<b>11,356</b>
Less: imputed interest	2,500
<b>Total operating lease liabilities</b>	<b>\$ 8,856</b>

## Guarantees

The Company agreed to act as a guarantor of Imugene's assumption of the MCAT lease through the lease expiration date of August 31, 2027. If Imugene fails to pay rent due on the MCAT Lease, the lessor may have contractual recourse against the Company.

As of December 31, 2023, the Company's guarantee consists of a contingent liability for aggregate minimum lease payments of approximately \$5.8 million. No contract liability for the Company's guarantee of Imugene's performance on the MCAT lease was recorded as of December 31, 2023, as it was not deemed probable that Imugene will be in default under the MCAT Lease.

## 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 financial condition, results of operations, or cash flows of the Company.

**NOTE 14: 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, 2023 and December 31, 2022.

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

	<u>Years Ended December 31,</u>	
	<u>2023</u>	<u>2022</u>
<b>Noncurrent deferred tax assets:</b>		
Net operating loss carryforwards	\$ 45,472	\$ 36,457
Contribution carryforwards	34	48
Lease liability	2,116	1,120
Deferred revenue	20,337	30,022
Capitalized R&D costs	28,732	15,893
Other assets	14,962	14,279
Tax credits	30,757	24,721
Less: valuation allowance	(139,133)	(121,372)
Total deferred tax assets, noncurrent	<u>3,277</u>	<u>1,168</u>
<b>Noncurrent deferred tax liability:</b>		
Investments and other	—	476
Deferred gain - Imugene	1,303	—
Right of use asset	1,974	692
Total deferred tax liabilities, noncurrent	<u>3,277</u>	<u>1,168</u>
Net deferred tax assets	\$ —	\$ —

As of December 31, 2023 and December 31, 2022, 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, 2023 of \$17.8 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, 2023 and December 31, 2022 and the amount computed by applying the statutory federal income tax rate to losses before income tax benefit are as follows (in thousands):

	<u>Year Ended December 31, 2023</u>		<u>Year Ended December 31, 2022</u>	
	<u>Amount</u>	<u>% of Pre-Tax Loss</u>	<u>Amount</u>	<u>% of Pre-Tax Loss</u>
Income tax expense at statutory rate	\$ (12,877)	21.0%	\$ (23,444)	21.0%
State income taxes, net of federal tax benefit	(1,774)	2.9%	(250)	0.2%
Non-deductible expenses	85	0.0%	33	0.0%
Stock compensation - nondeductible	681	(1.2%)	599	(0.5%)
Stock compensation - forfeitures	3,176	(5.2%)	2,233	(2.0%)
R&D and orphan drug credits	(6,078)	9.9%	(3,790)	3.4%
Other	657	(1.1%)	314	(0.3%)
Change in state tax rate	(1,632)	2.7%	(3,004)	2.7%
Change in valuation allowance	17,762	(29.0%)	27,309	(24.5%)
Income tax (benefit) expense	<u>\$ —</u>	<u>0.0%</u>	<u>\$ —</u>	<u>0.0%</u>

As of December 31, 2023, the Company had federal and state NOL carryforwards of approximately \$195.0 million and \$166.8 million respectively. As of December 31, 2022, the Company had federal and state NOL carryforwards of approximately \$159.5 million and \$119.1 million, respectively.

The federal NOL carryforward million carries forward indefinitely. The state NOL carryforwards begin to expire in 2027. As of December 31, 2023, the Company had federal and state R&D tax credits of \$17.2 million and an amount less than \$0.1 million, which begin to expire in 2029 and 2030, respectively. As of December 31, 2022, the Company had federal and state tax R&D credits of \$13.2 million and an amount less than \$0.1 million. As of December 31, 2023 and December 31, 2021, the Company had federal



Orphan Drug credits of \$13.5 million and \$11.6 million, respectively, which begin to expire in 2038. As of December 31, 2023 and December 31, 2022, the Company had federal contribution carryforwards of \$0.2 million which began to expire in 2023.

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 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, 2023 and December 31, 2022, 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 statements of operations. As of December 31, 2023 and December 31, 2022, 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 recognize 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, 2023 or December 31, 2022 and therefore, no GILTI tax has been recorded for the years then ended.

## **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.

## **NOTE 16: SUBSEQUENT EVENTS**

### *TG License Agreement*

On January 7, 2024, the Company entered into the TG License Agreement with TG Therapeutics, pursuant to which the Company granted TG Subsidiary certain exclusive and non-exclusive license rights to develop, manufacture, and commercialize the Company's allogeneic CAR T therapy azer-cel for autoimmune diseases and other indications outside of cancer (collectively referred to as licensed products). For a description of the TG License Agreement refer to Note 2, *Collaboration and License Agreements*.

### *Caribou Biosciences*

In February 2024, The Company announced that it had granted Caribou Biosciences, Inc. (“Caribou”), a leading CRISPR genome-editing cell therapy company, a non-exclusive, worldwide license, with the right to sublicense, to one of its foundational cell therapy patent families for use with CRISPR-based therapies in the field of human therapeutics. Under the terms of the agreement, the Company received an upfront payment and, upon commercialization by Caribou, will receive royalties on net sales of licensed products. In addition, for each occurrence of certain strategic transactions involving Caribou, the Company is eligible to receive a specific tiered milestone payment.

### *Reverse Stock Split*

On February 13, 2024, the Company effected the Reverse Stock Split, pursuant to which every 30 shares of the Company’s common stock issued or outstanding were automatically reclassified into one new share of common stock, subject to the treatment of fractional shares as previously described, without any action on the part of the holders. For a description of the Reverse Stock Split, refer to Note 1, *Description of Business and Summary of Significant Accounting Policies—Reverse Stock Split*.

### *Common Stock Offering*

In March 2024, the Company entered into an underwriting agreement relating to the issuance and sale of an aggregate of 2,500,000 shares of its common stock and warrants to purchase 2,500,000 shares of its common stock at a combined offering price of \$16.00 per share. Each warrant has an exercise price per share of \$20.00, is immediately exercisable and will expire on March 5, 2029. The offering was made pursuant to a registration statement on Form S-3. Gross proceeds from the transaction were \$40.0 million before deducting underwriting discounts and commissions and offering expenses of approximately \$2.9 million. In addition, the Company granted the underwriters a 30-day option to purchase up to an additional 375,000 shares of its common stock at \$16.00 per share, less underwriting discounts and commissions.

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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**  
Former Senior Vice President and Controller,  
Tapestry, Inc.

**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 Gene  
Therapy.

## **Corporate and Stockholder Information**

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**Investor Relations**  
Naresh Tanna  
Vice President, Investor Relations  
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**Annual Meeting of Stockholders**  
Tuesday, June 4, 2024  
11:00 a.m., Eastern Time  
Via live webcast

**Common Stock Listing**  
Nasdaq: DTIL

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