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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, 2024
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 001-41374

PEPGEN INC.

(Exact name of Registrant as specified in its Charter)

Delaware
(State or other jurisdiction of
incorporation or organization)
321 Harrison Avenue
Boston, MA
(Address of principal executive offices)

85-3819886
(I.R.S. Employer
Identification No.)
02118
(Zip Code)

Registrant’s telephone number, including area code: (781) 797-0979

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 \$0.0001 per share		PEPG	Nasdaq Global Select Market
Securities registered pursuant to Section 12(g) of the Act: None			
Indicate by check mark if the Registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☐ No ☒			
Indicate by check mark if the Registrant is not required to file reports pursuant to Section 13 or 15(d) of the Act. Yes ☐ No ☒			
Indicate by check mark whether the Registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the Registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐			
Indicate by check mark whether the Registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the Registrant was required to submit such files). Yes ☒ No ☐			
Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, smaller reporting company, or an emerging growth company. See the definitions of “large accelerated filer,” “accelerated filer,” “smaller reporting company,” and “emerging growth company” in Rule 12b-2 of the Exchange Act.			
Large accelerated filer	☐		Accelerated filer ☐
Non-accelerated filer	☒		Smaller reporting company ☒
			Emerging growth company ☒

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

Indicate by check mark whether the registrant has filed a report on and attestation to its management’s assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☐

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

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

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

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the Registrant, based on the closing price of the shares of common stock on Nasdaq Global Select Market on June 30, 2024, was \$272.9 million. The number of shares of Registrant’s Common Stock outstanding as of February 18, 2025 was 32,692,388.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant’s Definitive Proxy Statement relating to its 2025 Annual Meeting of Stockholders to be filed hereafter are incorporated by reference into Part III of this Annual Report on Form 10-K where indicated.

Auditor Firm Id: 185 Auditor Name: KPMG LLP Auditor Location: Phoenix, AZ, USA

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SPECIAL NOTE REGARDING FORWARD LOOKING STATEMENTS

This Annual Report on Form 10-K, or 10-K, contains express or implied forward-looking statements that are based on our management's belief and assumptions and on information currently available to our management and which are made pursuant to the safe harbor provisions of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. Although we believe that the expectations reflected in these forward-looking statements are reasonable, these statements relate to future events or our future operational or financial performance, and involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by these forward-looking statements. Forward-looking statements in this 10-K include, but are not limited to, statements about:

- the initiation, timing, progress, results, and cost of our research and development programs and our current and future preclinical studies and clinical trials, including statements regarding the timing of initiation and completion of studies or trials and related preparatory work, and the period during which the results of our clinical trials will become available;
- our ability to efficiently develop our existing product candidates and discover new product candidates;
- our ability to successfully manufacture our investigational drug substances and drug product for preclinical use, for clinical trials and on a larger scale for commercial use, if our investigational drug candidates are approved;
- our ability to obtain funding for our operations necessary to complete further development and commercialization of our product candidates;
- our ability to obtain and maintain regulatory approval of our product candidates;
- our ability to commercialize our product candidates, if approved;
- the pricing and reimbursement of our product candidates, if approved;
- the implementation of our business model, and strategic plans for our business and product candidates;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our product candidates and our technology platform;
- estimates of our future expenses, revenues, capital requirements, and our needs for additional financing;
- the size and growth potential of the markets for our product candidates, and our ability to serve those markets;
- our financial performance;
- the rate and degree of market acceptance of our product candidates;
- regulatory developments in the United States, or U.S., and foreign countries;
- our ability to contract with third-party suppliers and manufacturers and their ability to perform adequately, and our ability to identify and contract with alternative third-party suppliers and manufacturers in a timely manner and on reasonable terms, if needed;
- our ability to produce our products or product candidates with advantages in turnaround times or manufacturing cost;
- the success of competing therapies that are or may become available;
- our ability to attract and retain key research and development or management personnel;
- the impact of laws and regulations;
- developments relating to our competitors and our industry;
- the effects of any epidemics or pandemics, including mitigation efforts and economic effects, on any of the foregoing or other aspects of our business operations, including but not limited to our preclinical studies and clinical trials and any future studies or trials; and
- other risks and uncertainties, including those listed under the caption "*Risk Factors.*"

In some cases, you can identify forward-looking statements by terminology such as "may," "will," "should," "expects," "intends," "plans," "anticipates," "believes," "estimates," "predicts," "potential," "continue" or the negative of these terms or other

comparable terminology. These statements are only predictions, and are subject to change due to known and unknown risks, uncertainties, and other factors, which are, in some cases, beyond our control and which could materially affect results. Factors that may cause actual results to differ materially from current expectations include, among other things, those listed under the section titled “*Risk Factors*” and elsewhere in this 10-K. If one or more of these risks or uncertainties occur, or if our underlying assumptions prove to be incorrect, actual events or results may vary significantly from those implied or projected by the forward-looking statements. No forward-looking statement is a guarantee of future performance. 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 10-K and the documents that we reference in this 10-K and have filed with the U.S. Securities and Exchange Commission, or the SEC, completely and with the understanding that our actual future results may be materially different from any future results expressed or implied by these forward-looking statements.

The forward-looking statements in this 10-K represent our views as of the date of this 10-K. We anticipate that subsequent events and developments will cause our views to change. However, while we may elect to update these forward-looking statements at some point in the future, we have no current intention of doing so except to the extent required by applicable law. You should therefore not rely on these forward-looking statements as representing our views as of any date subsequent to the date of this 10-K.

In addition, statements that “we believe” and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this 10-K, and while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain.

This 10-K also contains estimates, projections and other information concerning our industry, our business and the markets for our programs and product candidates. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances that are assumed in this information. Unless otherwise expressly stated, we obtained this industry, business, market, and other data from our own internal estimates and research as well as from reports, research surveys, studies, and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data and similar sources. While we are not aware of any misstatements regarding any third-party information presented in this 10-K, their estimates, in particular, as they relate to projections, involve numerous assumptions, are subject to risks and uncertainties and are subject to change based on various factors, including those discussed under the section titled “*Risk Factors*” and elsewhere in this 10-K.

TRADEMARKS

This 10-K contains references to our trademarks and to trademarks belonging to other entities. Solely for convenience, trademarks and trade names referred to, including logos, artwork and other visual displays, may appear without the ® or TM symbols, but such references are not intended to indicate, in any way, that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto. We do not intend our use or display of other companies’ trade names or trademarks to imply a relationship with, or endorsement or sponsorship of us by, any other companies.

SUMMARY OF RISK FACTORS

Our business is subject to numerous risks and uncertainties that you should be aware of in evaluating our business. These risks include, but are not limited to, the following:

- We have incurred significant losses since our inception, have no products approved for sale and we expect to incur losses for the foreseeable future.
- We will need to raise substantial additional funding. If we are unable to raise capital when needed, we could be forced to delay, scale back, or discontinue our product development programs or future commercialization efforts.
- We are early in our development efforts. We have only completed a Phase 1 clinical trial and initiated Phase 2 clinical trials for our first product candidate, as well as initiated an additional Phase 1 clinical trial and more recently, a Phase 2 clinical trial of a second product candidate, and as a result it will be years before we commercialize a product candidate, if ever. If we are unable to advance our product candidates through preclinical studies and clinical trials, obtain marketing approval and ultimately commercialize them, or experience significant delays in doing so, our business will be materially harmed.
- Our business is highly dependent on the clinical advancement of our programs and modalities and is especially dependent on the success of our lead product candidates, PGN-EDO51 and PGN-EDODM1. Delay or failure to advance programs or modalities, including PGN-EDO51 and PGN-EDODM1, including as a result of a clinical hold or other regulatory action, could adversely impact our business.
- Preclinical and clinical development involves a lengthy and expensive process with an uncertain outcome, and the results of preclinical and clinical studies, including studies of PGN-EDO51, PGN-EDODM1 and other research candidates, are not necessarily predictive of the results of later preclinical studies and any clinical trials of our product candidates. Our product candidates may not have favorable results in clinical trials, if any, or receive regulatory approval on a timely basis, if at all.
- Substantial delays in the commencement, enrollment or completion of our clinical trials and advancement of our clinical trials, including as a result of clinical hold or other regulatory action, or failure to demonstrate safety and efficacy to the satisfaction of applicable regulatory authorities could prevent us from commercializing product candidates we determine to develop on a timely basis, if at all.
- We rely, and expect to continue to rely, on third parties to conduct some or all aspects of our product manufacturing, research, preclinical and clinical testing, and these third parties may not perform satisfactorily. If we have to replace one or more of these third parties, we may be unable to enter into new agreements in a timely manner or on reasonable terms, if at all.
- We face significant competition, and if our competitors develop technologies or product candidates more rapidly than we do or their technologies or product candidates are more effective or have more favorable safety or tolerability profiles, our business and our ability to develop and successfully commercialize products may be adversely affected.
- If we are unable to obtain and maintain patent protection for our Enhanced Delivery Oligonucleotide platform, therapeutic development candidates or programs and/or other proprietary technologies we develop, or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize products and technology similar or identical to ours, and our ability to successfully commercialize our therapeutic product candidates or programs and other proprietary technologies we may develop may be adversely affected.
- We expect to expand our headcount to support our development and regulatory capabilities and potentially implement sales, marketing and distribution capabilities, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.
- Our future success depends on our ability to retain key executives and to attract, retain and motivate qualified personnel.
- The price of our common stock is volatile and fluctuates substantially, which could result in substantial losses for holders of our common stock.

The summary risk factors described above should be read together with the text of the full risk factors below in the section titled “*Risk Factors*” in Part I, Item 1.A. and the other information set forth in this 10-K, as well as in other documents that we file with the SEC. The risks summarized above or described in full below are not the only risks that we face. Additional risks and uncertainties not precisely known to us, or that we currently deem to be immaterial, may also materially adversely affect our business, financial condition, results of operations and future growth prospects.

PART I

Item 1. Business.

Overview

PepGen Inc. (also referred to as “PepGen,” “we,” “our” or “us”) is a clinical-stage biotechnology company advancing the next generation of oligonucleotide therapeutics with the goal of transforming the treatment of severe neuromuscular and neurologic diseases. Our proprietary Enhanced Delivery Oligonucleotide, or EDO, platform is founded on over a decade of research and development and leverages cell-penetrating peptides, or CPPs, to improve the uptake and activity of conjugated oligonucleotide therapeutics. Our EDO peptides are engineered to optimize tissue penetration, cellular uptake and nuclear delivery, and in preclinical studies we have observed their ability to transport oligonucleotides into a broad range of target tissues, including smooth, skeletal, and cardiac muscle. We have also demonstrated robust delivery and activity of oligonucleotides to skeletal muscle in our early clinical trials with our investigational therapeutics, PGN-EDO51 and PGN-EDODM1. Furthermore, the high levels of pharmacological activity observed in preclinical and clinical studies support our belief that our EDO platform technology has the potential to deliver therapeutic agents to the nucleus of the target cells. Using these EDO peptides, we are generating a pipeline of oligonucleotide product candidates that target the root cause of serious diseases.

We are initially focused on addressing the underlying cause of Duchenne muscular dystrophy, or DMD, and myotonic dystrophy type 1, or DM1, that have high unmet need. Our current pipeline depicted below consists of two clinical stage programs - PGN-EDO51 for DMD patients who are amenable to exon 51 skipping and PGN-EDODM1 for DM1 patients, as well as a number of additional preclinical stage programs. We anticipate expanding this pipeline over time to include other neuromuscular targets as well as potential opportunities in neurologic diseases.

INVESTIGATIONAL CANDIDATES	CLINICAL PROGRAMS	INDICATIONS	PRECLINICAL	PHASE 1	PHASE 2	PIVOTAL
PGN-EDO51	 Connect	DMD – Exon 51				
PGN-EDODM1	 Freedom	DM1 – DMPK				
PGN-EDO53		DMD – Exon 53				


Research

- DMD Exon 45, Exon 44
- Additional neuromuscular diseases
- Neurological diseases

PGN-EDO51

We are developing PGN-EDO51 to treat DMD patients whose mutations are amenable to an exon 51-skipping approach. We completed a first-in-human Phase 1 clinical trial in healthy volunteers, or HVs, with PGN-EDO51 in the third quarter of 2022. Our ongoing clinical development program for PGN-EDO51 is comprised of two parallel Phase 2 studies of PGN-EDO51 in DMD patients. The first study, CONNECT1-EDO51, or CONNECT1, is an ongoing open-label, multiple ascending dose, or MAD, study in boys and young men living with DMD being conducted in Canada. The CONNECT1 study was designed to provide proof-of-concept for our EDO platform and PGN-EDO51, as well as inform the design and conduct of our CONNECT2-EDO51, or CONNECT2, study. We reported initial clinical data from CONNECT1 in the third quarter of 2024 from the 5 mg/kg dose cohort which we believe demonstrate a favorable emerging safety profile and promising early exon skipping and dystrophin production levels. The 10 mg/kg cohort is fully enrolled and participants in the 5 mg/kg cohort are continuing to dose at that level in the long-term extension, or LTE, phase of the study. We expect to report clinical data from the 10 mg/kg cohort by the end of the third quarter of 2025. We have received communication from Health Canada that dosing of participants in the 5 and 10 mg/kg cohorts may continue at their current dose levels. Health Canada has requested additional information from us to address its safety concerns before any further dose escalation or enrollment of any additional participants at the current dose levels. We are working with Health Canada to address its questions.

The second study, CONNECT2, is a randomized, double-blind, placebo-controlled MAD study. The CONNECT2 study is open in the U.K., with plans to evaluate opening the study in other geographies subject to regulatory authorizations. In December 2024, we announced that we received a clinical hold notice from the U.S. Food and Drug Administration, or FDA, regarding our investigational new drug, or IND, application to initiate the CONNECT2 study in the U.S. We are working with the FDA to address its questions regarding supportive data for the dosing levels planned for the patient population.

The CONNECT2 study has been designed and optimized based on learnings from the CONNECT1 study and, together with data from the CONNECT1 study, is intended to support a potential accelerated approval pathway for PGN-EDO51, subject to regulatory authority feedback. Based on the high levels of exon skipping observed in both the Phase 1 trial in HVs and the early results from the CONNECT1 trial at 5 mg/kg in DMD patients, we believe that higher doses and a longer duration of treatment with PGN-EDO51 may lead to therapeutically relevant accumulation of *DMD* exon 51-skipped transcript and an associated increase in dystrophin protein in patients, which may in turn drive meaningful clinical benefit for those who live with this devastating, progressive, life-shortening disease.

PGN-EDODM1

We are also developing PGN-EDODM1 for the treatment of DM1 and are utilizing what we believe to be a unique mechanism of action and a different delivery approach compared to other approaches in more advanced stages of clinical development. The therapeutic oligonucleotide component of PGN-EDODM1 is engineered to bind to the pathogenic cytosine-uracil-guanine, or CUG repeat expansion present in the myotonic dystrophy protein kinase, or *DMPK*, messenger RNA, or mRNA, of DM1 patients, thus reducing the ability of these expanded trinucleotide repeats to bind and sequester RNA binding proteins including MBNL1, a critical RNA splicing factor. The liberation of MBNL1 in turn leads to the correction of downstream mis-splicing events that drive the pathology of DM1. We believe this approach, which is not designed to knock down or degrade *DMPK* transcript, has the potential to selectively and directly address the underlying genetic defect central to this disease. In a DM1 mouse model, the HSA^{LR} mouse, following single and repeat dosing of PGN-EDODM1 every four weeks, we observed robust correction of mis-splicing and resolution of myotonia.

Our clinical development program for PGN-EDODM1 includes two ongoing studies. FREEDOM-DM1, or FREEDOM, is a Phase 1 multinational, randomized, double-blind, placebo-controlled, single ascending dose, or SAD, study, designed to assess PGN-EDODM1's safety and pharmacokinetics. In addition, the study will explore the potential impact of PGN-EDODM1 on splicing correction, and functional outcome measures in DM1 patients. On February 24, 2025, we reported initial data from the 5 mg/kg and 10 mg/kg dose cohorts in this study. PGN-EDODM1 was observed to have a favorable emerging safety profile and robust splicing correction in a dose-dependent manner in the 5 and 10 mg/kg dose cohorts. The 15 mg/kg cohort is currently enrolling participants and we have begun dosing at this level. We anticipate reporting data from this cohort in the second half of 2025. The second study, FREEDOM2-DM1, or FREEDOM2, is a Phase 2 multinational, randomized, double-blind, placebo-controlled MAD study in DM1 patients. We have received clearance from Health Canada and the Medicines and Healthcare products Regulatory Agency, or MHRA, to initiate FREEDOM2 in Canada and the U.K., respectively. This study is currently dosing participants in the 5 mg/kg dose cohort and we expect to report data from this cohort in the first quarter of 2026.

Additional Discovery and Preclinical Programs

In addition to these lead clinical stage programs, we are evaluating EDO candidates for additional DMD sub-populations amenable to skipping of other exons, including exon 53, 45 and 44. We have previously reported robust exon 53-skipping levels following either a single dose or multiple doses in non-human primates, or NHPs, for our PGN-EDO53 program. We have also initiated research efforts for additional indications, including neuromuscular diseases and neurologic disorders.

Our EDO Platform

Background on Oligonucleotide Therapeutics

Oligonucleotide therapeutics consist of small single or double stranded segments of deoxyribonucleic acid, or DNA, or ribonucleic acid, or RNA, molecules that are made up of nucleotides that bind to their targets via complementary Watson-Crick base pairing thereby modulating the expression of their target DNA or RNA sequence, thereby addressing the root cause of many diseases. Upon binding to their target sequence, oligonucleotides can modulate function through the modulation of RNA expression and processing. The mechanisms of action of these medicines include interference with gene expression; degradation of toxic RNA species; alteration of gene translation; interference with interactions between RNA and other nucleic acids or proteins; endogenous human adenosine deaminase acting on RNA, or ADAR; site-directed RNA editing; and modulation of the splicing of transcripts. Each of these approaches can lead to profound biological effects. The development of oligonucleotide therapeutics has enabled the targeting of a diverse set of diseases that have proven difficult to treat through other approaches due to their high degree of specificity to target pathogenic mutations.

Oligonucleotide therapeutics have demonstrated clinical benefit and been approved for the treatment of multiple diseases, such as spinal muscular atrophy, DMD, familial hypercholesterolemia and hereditary transthyretin-mediated amyloidosis. These approved drugs span two classes – ASOs, which are short, synthetic, single-stranded oligonucleotides, and small interfering RNAs, or siRNAs, which are double-stranded oligonucleotides. ASOs and siRNAs both bind their target mRNAs or pre-mRNAs but differ in their respective modes of action. ASOs are designed to either (i) degrade target RNA species through an RNase-H-mediated process, or (ii) modulate RNA-RNA and/or RNA-protein interactions through a steric blocking mechanism. In contrast, siRNAs are designed to silence or knockdown a particular mRNA through the RNA interference, or RNAi, pathway.

ASOs are typically synthetic molecules that may contain modified nucleotide bases, sugars and phosphate linkages designed to overcome the historical limitations of unmodified oligonucleotides, including instability, immunogenicity and a poor pharmacological profile. Many approved oligonucleotides incorporate a modified oligonucleotide backbone in which the phosphate and ribose sugars are replaced by phosphorodiamidate morpholino groups, or PMOs. The resulting PMOs are resistant to multiple hydrolases in serum, while their uncharged nature ensures that they do not interact strongly with proteins in a nonspecific way. PMOs have shown

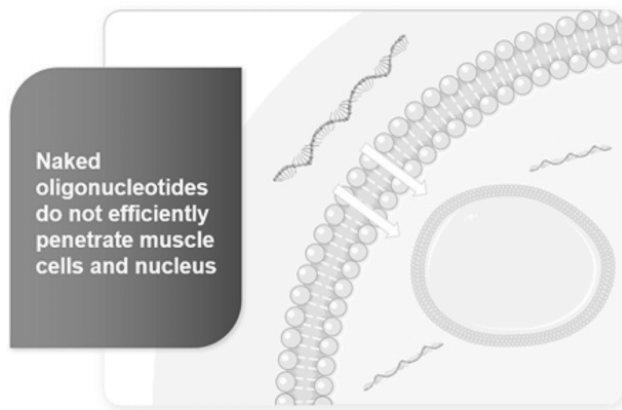
promising results in early-stage preclinical studies and have become marketed products for the treatment of a host of diseases. For example, EXONDYS 51® (eteplirsen), marketed by Sarepta Therapeutics, Inc., or Sarepta, is a PMO that was approved in 2016 for individuals with DMD who are amenable to exon 51 skipping but has left much room for improvement given its relatively low tissue and cell penetration and minimal induction of dystrophin production.

The Challenge of Oligonucleotide Delivery

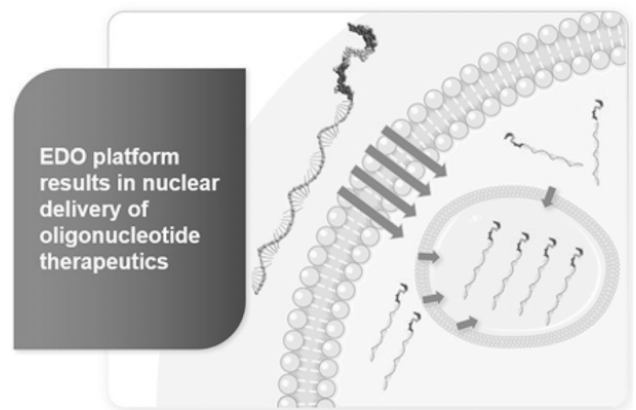
In order for oligonucleotide therapeutics to exert their intended effect, they must first gain access to the nucleus where mRNAs are synthesized and processed. Historically, the delivery of oligonucleotides to the interior of the cell proved challenging due to their high molecular weight and the lack of a specific mechanism to facilitate their transport across the cell membrane and escape the endosome to enter the cytoplasm and nucleus. Several methods have been developed to increase the cellular uptake of oligonucleotides, the most clinically advanced of which is the covalent attachment of CPPs. CPPs are designed to facilitate the transport of oligonucleotides across the plasma membrane, thus allowing these cargo species to reach their eventual site of action in the nucleus. We believe that these capabilities are critical in enabling oligonucleotides to exert their intended therapeutic effect within the cell. Early research into CPPs showed that simple peptides consisting primarily of multiple arginine residues could increase the cellular uptake of oligonucleotides and increase their activity in modulating RNA splicing. However, a considerable number of these early CPPs were found to be highly toxic in animal models, and in many instances, there existed a direct correlation between toxicity and activity, which limited the clinical translation and development of these first-generation delivery vectors.

Our Approach: A Solution for the Oligonucleotide Delivery Challenge

The Challenge of Oligonucleotides



EDO Platform Solution



Our EDO platform is based on novel CPP technology. We engineered our proprietary EDO technology to optimize cellular uptake and nuclear delivery, which we believe may enhance therapeutic activity and improve the tolerability of oligonucleotide therapeutics. This technology is founded on over a decade of research and development conducted in the academic laboratories of our founders Michael Gait, Ph.D. at the Medical Research Council Laboratory of Molecular Biology in Cambridge, United Kingdom, or MRC, and Professor Matthew Wood, M.D., Ph.D. at the University of Oxford, United Kingdom.

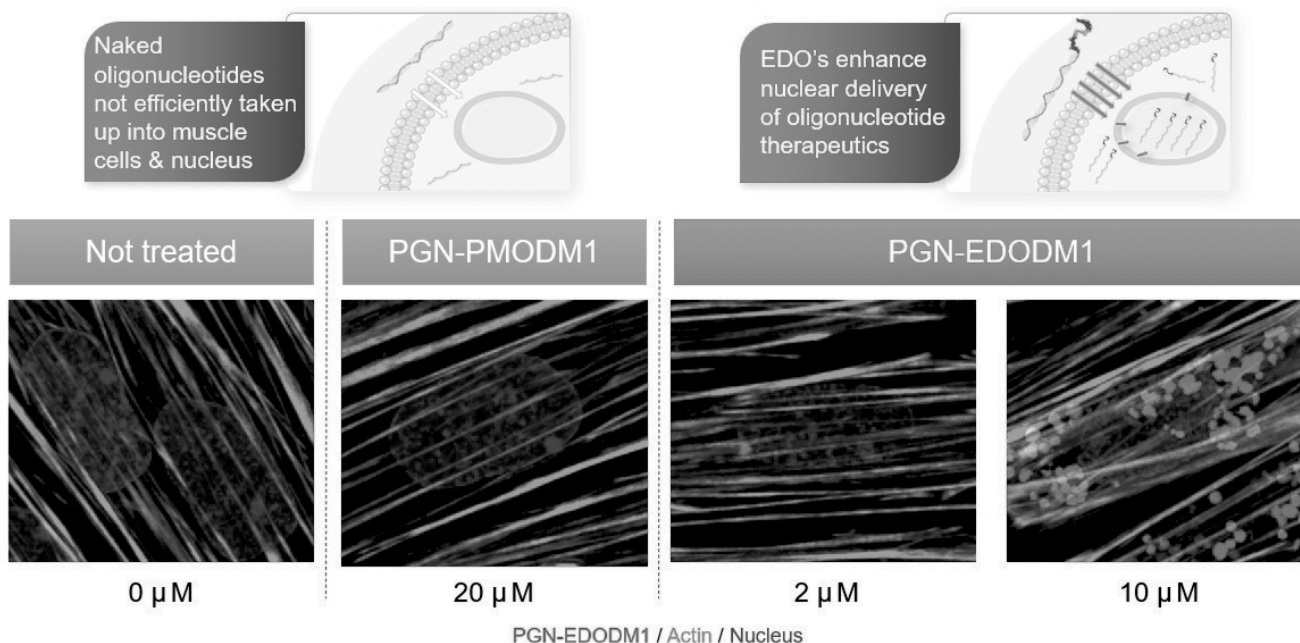
Our EDO platform peptides possess the following key structural characteristics:

- Two positively charged, arginine-rich regions, one at the N-terminus and the other at the C-terminus interspersed with non-natural amino acids to confer greater peptide stability;
- A central core rich in hydrophobic residues that separates the arginine-rich regions and is distinct from the older generation of CPPs, known as PIP peptides, and contributes to endosomal escape; and
- A linear peptide sequence with a length of less than 20 amino acids designed to be non-immunogenic.

Our EDO peptides were developed through an iterative optimization process that selected simultaneously for: biodistribution to muscle tissue; high cellular uptake; endosomal escape, where the therapeutic agent is released from the endosomes, a sub-cellular organelle, in a functional form and delivered to the cell nucleus; and acceptable tolerability. We utilize PMOs in our approach, and these therapeutic cargos are conjugated to one of our optimized, proprietary, novel EDO peptides to generate our lead EDO product candidates - peptide conjugated PMOs, or PPMOs. We intend to continue to build and develop this platform technology to enable us to expand into new therapeutic areas.

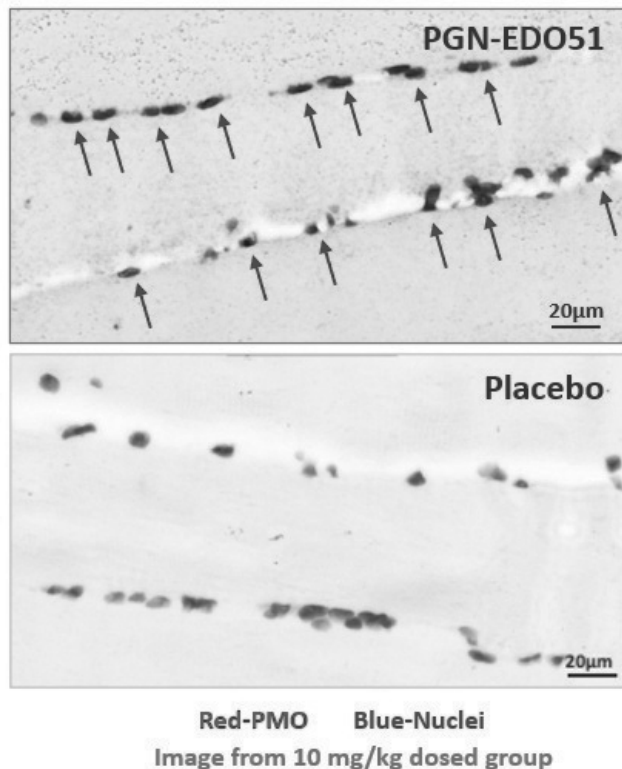
We believe that our therapeutic candidates may offer the following advantages with the goal of enabling the safe and efficient delivery of oligonucleotide cargos:

- Enhanced delivery to the nucleus of skeletal muscle.** We have observed in preclinical and early clinical studies that our peptides demonstrated enhanced delivery of their cargo oligonucleotide therapeutics to the nucleus of skeletal muscle. We believe that EDO peptides have the potential to promote endosomal escape and facilitate the robust delivery of cargo oligonucleotides to the cell nucleus. We have now shown in *in vitro* and in NHP models, and more recently in early clinical studies, that our EDO technology can mediate higher uptake of oligonucleotide in the nucleus.



PGN-EDODM1 treatment results in higher nuclear delivery of PMO. *Immortalized myoblasts from a healthy individual or a DM1 patient with 2600 CTG repeats were cultured then differentiated for 4 days into myotubes and then treated with fluorescently tagged PGN-PMODM1 (PMO) or PGN-EDODM1 (PPMO) at concentrations detailed above. Cells were visualized by confocal microscopy 24h after treatment.*

- Encouraging activity and favorable emerging safety profile observed in a Phase 1 HV clinical study and in early data from Phase 2 clinical study of PGN-EDO51 and Phase 1 clinical study of PGN-EDODM1.**
 - In our Phase 1 clinical study of PGN-EDO51 in HVs, we observed high levels of mean exon skipping in skeletal muscle following a single dose. Post hoc analyses showed high exon skipping levels that correlated with high uptake of PGN-EDO51 in the myocytes and nuclei.



HVs were dosed with placebo or 10 mg/kg of PGN-EDO51 via IV infusion. Representative image from one subject's bicep samples collected at day 10 and assessed for PGN-EDO51 levels in post hoc in situ hybridization analysis using probe targeting the PMO sequence. Arrows denote nuclei positive for PMO.

- o In our Phase 2 CONNECT1 clinical study of PGN-EDO51 in DMD patients, we observed high levels of exon 51 skipping in skeletal muscle after three months and four doses at 5 mg/kg. We believe PGN-EDO51 has been observed to have a favorable emerging safety profile at 5 mg/kg and 10 mg/kg through January 23, 2025.
- o In our Phase 1 FREEDOM study of PGN-EDODM1 in DM1 patients, we observed robust splicing correction in skeletal muscle at the 5 and 10 mg/kg dose levels, which we believe further supports the platform potential of EDOs across multiple neuromuscular diseases.
- **Robust, scalable and cost-efficient manufacturing that does not require cell-based processes.** We have developed a modular manufacturing process that is highly scalable, easily characterizable, and utilizes readily available building blocks. This process is fully synthetic in nature and does not rely on microbial fermentation, thus substantially reducing the risk of introducing microbial DNA or protein into our product candidates.
- **Efficient development of pipeline therapeutic candidates enabled by use of a single EDO peptide across all our initial programs.** We currently utilize the same EDO delivery peptide across all of our programs. We intend to apply our knowledge and learnings from our current lead programs in order to efficiently pursue our future programs, and we will additionally aim to take advantage of economies of scale in our manufacturing processes.

Our Strategy

Our goal is to become a leading biopharmaceutical company focused on the development and commercialization of oligonucleotide therapies to transform the lives of patients with severe neuromuscular and neurologic diseases. We aim to accomplish this goal by implementing the following strategies:

- **Advance PGN-EDODM1 through clinical trials and potential regulatory approval.** We are developing PGN-EDODM1, an EDO peptide conjugated to a PMO therapeutic cargo to treat DM1 patients and have observed robust pharmacological activity in preclinical models with both long and short cytosine-thymine-guanine, or CTG repeats. In the FREEDOM Phase 1 clinical study of PGN-EDODM1 in DM1 patients, PGN-EDODM1 was observed to have a favorable emerging safety profile and robust splicing correction in a dose-dependent manner in the 5 and 10 mg/kg dose cohorts.
- **Advance PGN-EDO51 through clinical trials and potential regulatory approval.** We are developing PGN-EDO51, which utilizes the same EDO peptide as PGN-EDODM1 conjugated to a PMO therapeutic cargo to treat DMD patients whose mutations are amenable to an exon 51-skipping approach. There is no cure for DMD and approved exon-skipping therapies or advanced stage exon-skipping investigational candidates for patients who are amenable to exon 51 skipping are

thought to have limited impact on disease progression due to low levels (<5%) of unadjusted dystrophin production. In the CONNECT1 Phase 2 clinical study of PGN-EDO51 in DMD patients, the 5 mg/kg low dose of PGN-EDO51 was observed to have a favorable emerging safety profile and produced mean exon skipping of 2.15% at week 13 compared to baseline, measured by RT-PCR, and generated encouraging levels of dystrophin production.

- **Leverage the full potential of our EDO technology to expand into treatment of additional DMD patient populations as well as new neuromuscular and neurological disease areas.** Given the potential of the EDO technology to efficiently deliver nucleic acid payloads such as PMOs to skeletal muscle, cardiac tissue and diaphragm, we are looking to develop disease-modifying peptide-conjugated oligonucleotide candidates for the potential treatment of other neuromuscular and neurological indications, including other DMD populations.
- **Utilize the modular nature of our EDO platform to evaluate new cargos and peptide technologies.** We believe that our EDO technology has the potential to facilitate the delivery of multiple classes of nucleic acid payloads, including other oligonucleotide therapeutics, and longer-term, we intend to expand the scope of the cargos that can be delivered by our EDO platform as part of our ongoing platform development work.
- **Maximize the value of our pipeline and our EDO platform by selectively exploring strategic collaborations.** We have a disciplined strategy to maximize the value of our pipeline and currently have worldwide development and commercial rights to all of our product candidates. Given the potential of our EDO platform, we may opportunistically enter into strategic collaborations around certain geographies, targets or programs. We may seek to build such relationships where we believe the resources and expertise of a third-party pharmaceutical or biotechnology company could be beneficial to the development or commercialization of our product candidates or to the expansion of our platform capabilities.

Our Portfolio

We are harnessing the power of our EDO platform to generate a pipeline of oligonucleotide therapeutic candidates. Our EDO conjugates have been engineered to successfully target the root cause of serious diseases while maintaining a tolerability profile that is acceptable for clinical use. We are initially focused on addressing neuromuscular indications and are building a portfolio of therapeutic candidates to address the underlying genetic mutations found in DMD and DM1, with our current pipeline being comprised of multiple programs, two clinical and several preclinical.

In the future, we anticipate expanding this pipeline to include other neuromuscular targets, along with potential opportunities in neurologic indications, and we will seek to leverage the modular, scalable nature of our EDO technology to support our expansion into these new therapeutic areas. We have worldwide development and commercialization rights to all our programs.

PGN-EDO51

Overview

Our initial product candidate is PGN-EDO51, an EDO peptide conjugated to a PMO, that we are developing for the treatment of DMD patients with mutations amenable to an exon 51-skipping approach. An exon is a segment of a gene that, together with other exons, contains the genetic code that is translated into a protein. Exon skipping is a therapeutic mechanism that enables mutations in the gene to be bypassed, thereby repairing this code or reading frame and enabling production of a truncated, yet functional version of the target protein. PGN-EDO51 is designed to splice out exon 51 and potentially additional exons depending on the mutation of the dystrophin pre-mRNA, resulting in the restoration of the open reading frame of the dystrophin transcript and production of an internally deleted, yet functional dystrophin protein. We have completed a Phase 1 clinical trial of PGN-EDO51 in HVs, in which we observed high levels of exon skipping in humans following a single dose. In this Phase 1 clinical trial, PGN-EDO51 was observed to be generally well-tolerated at potentially clinically relevant dose levels.

We are currently advancing PGN-EDO51 in two Phase 2 studies, CONNECT1 and CONNECT2. In July 2024, we reported initial data from CONNECT1, an open-label MAD study in DMD patients amenable to an exon 51-skipping approach underway in Canada. PGN-EDO51 was observed to have a favorable emerging safety profile and encouraging exon skipping levels and dystrophin production at the starting dose of 5 mg/kg. We have fully enrolled the 10 mg/kg dose cohort and participants in the 5 mg/kg cohort are continuing to dose at that level in the LTE phase of the study. We expect to report initial safety, exon skipping and dystrophin production data from the 10 mg/kg cohort by the end of the third quarter of 2025. We have received communication from Health Canada that dosing of participants in the 5 and 10 mg/kg cohorts may continue at their current dose levels. Health Canada has requested additional information from us to address its safety concerns before any further dose escalation or enrollment of any additional participants at the current dose levels. We are working with Health Canada to address its questions. Our second Phase 2 study of PGN-EDO51, CONNECT2, is a randomized, placebo-controlled MAD study, which, together with data from the CONNECT1 study, is intended to support a potential accelerated approval pathway for PGN-EDO51, subject to regulatory authority feedback. The CONNECT2 study is open in the U.K., with plans to evaluate opening the study in other geographies subject to regulatory authorizations. In December 2024, we announced that we received a clinical hold notice from the FDA regarding our IND application to initiate the CONNECT2 study in the US. We are working with the FDA to address its questions regarding supportive data for the dosing levels planned for the patient population.

The FDA has granted both orphan drug designation and rare pediatric disease designation, or RPDD, for PGN-EDO51 for the treatment of DMD patients who are amenable to exon 51 skipping.

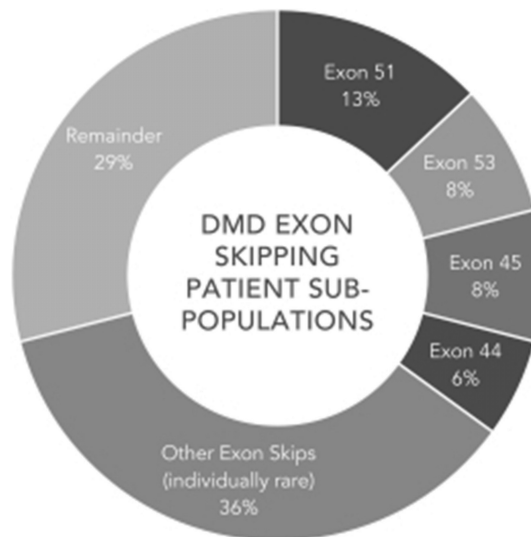
Disease Background and Prevalence

DMD is a debilitating X-linked recessive, progressive, muscle-wasting disease that predominantly affects boys. It is one of the most prevalent rare genetic diseases globally, with an incidence of up to 1 in 3,500 to 5,000 live male births, and it is invariably fatal by young adulthood. There are up to 15,000 DMD patients in the U.S., approximately 25,000 DMD patients in Europe and approximately 5,000 in Japan. DMD is caused by mutations in the gene encoding dystrophin, a protein necessary for normal muscle function. The primary role of dystrophin is as a shock absorber, and this protein allows muscle cells to retain their structural integrity while under mechanical stress. In the absence of dystrophin, muscle fibers are no longer protected from the mechanical forces of contraction, which leads to cell death, fibrotic tissue formation and muscle degeneration resulting in loss of ambulation.

Early symptoms of disease include difficulty walking or jumping, loss of balance, and increased fatigue when compared to healthy peers. By their mid-teenage years, most DMD patients will need to use a wheelchair on a regular basis. As the disease progresses, life-threatening heart and respiratory conditions become common. Dilated cardiomyopathy – a condition where the cardiac muscle becomes weakened and the chambers of the heart are enlarged – often arises, and heart failure is a leading cause of death in DMD patients. Pulmonary function also becomes progressively impaired as the dystrophic process affects respiratory muscles, including the diaphragm, leading to significant morbidity and mortality. DMD patients ultimately succumb to cardiac and respiratory failure in early adulthood, with a mean lifespan of approximately 25 years. Therefore, the restoration of dystrophin is a compelling therapeutic strategy, and a number of therapeutic modalities have been explored with this goal in mind. However, the nature of the *DMD* gene, the range of mutations implicated in DMD, and the large size of the dystrophin protein itself provide considerable obstacles to this approach.

The *DMD* gene, at 2.1 million base pairs and 79 exons, is one of the largest in the human genome. Over 6,000 mutations are known, and the gene has a relatively high natural mutation rate, with approximately 1 in 3 DMD cases arising due to a *de novo* mutation. There is no one mutation that is highly prevalent, and this factor provides a considerable challenge for therapeutics looking to target the root genetic cause of this debilitating disease.

That said, mutations in the dystrophin gene are not random, with hotspots of mutations existing between exons 45-53 and to a lesser extent between exons 2-20. It is thought that 13% of patients with DMD have mutations that are amenable to treatment with an exon 51-skipping approach, and thus the estimated exon 51 patient population is approximately 2,000 in the U.S., 3,200 in Europe and 700 in Japan.



Breakdown of DMD population by amenability to treatment with exon skipping therapeutics.

Current Approaches and Unmet Needs

There is no cure for DMD and approved exon-skipping therapies or advanced stage exon-skipping investigational candidates for patients who are amenable to exon 51 skipping are thought to have limited impact on disease progression due to low levels (<5%) of unadjusted dystrophin production. Corticosteroids are the mainstay of pharmacologic treatment for DMD as they have been shown to temporarily improve muscle strength, prolong the period of ambulation and slow the progression of this disease. However, glucocorticoid use is associated with well-known adverse effects, such as weight gain, stunted growth, weakening of bone structure, high blood pressure, diabetes, psychological effects, skin thinning and an increased risk of infection.

Several approaches have been taken to address groups of mutations in the dystrophin gene, one of which is to alter the processing of the dystrophin mRNA. A number of DMD patients suffer from mutations that result in the disruption of the reading frame of the DMD transcript, which in turn leads to an absence of the dystrophin protein. Using an ASO, the mRNA splicing process in the nucleus can be altered to skip over a select exon, allowing the open reading frame to be restored. This exon skipping approach

results in the subsequent generation of dystrophin protein isoform which, although internally deleted, retains much of its function and can thus protect muscle tissue against further contraction-induced damage.

Several unconjugated, or “naked” ASOs have been approved to treat DMD, including eteplirsen, marketed as EXONDYS 51 by Sarepta for the treatment of mutations amenable to an exon 51-skipping approach. This drug received accelerated approval from the FDA on the basis of an increase of less than 1% in the expression of dystrophin, with this readout being considered a valid surrogate endpoint under the accelerated approval regulatory pathway. Published observational studies of small numbers of patients on EXONDYS 51 appear to show somewhat slower disease progression than historical controls. However, at this level of dystrophin, this therapeutic has yet to formally establish evidence of clinical benefit through rigorously powered and adequately controlled clinical trials with functional endpoints. EXONDYS 51 has not been approved in Europe, or in Japan on the basis of this minimal degree of dystrophin restoration as a surrogate endpoint. Several companies are also developing antibody-oligonucleotide conjugates with the aim of enhancing the delivery and activity of their cargo therapeutics. These groups utilize both antigen-binding fragments, or Fabs, and monoclonal antibodies, or mAbs, as delivery vectors, to target specific cell surface receptors. We believe our EDO platform offers significant potential benefits over such approaches.

In addition, several companies are developing gene therapies to treat DMD. These include Sarepta’s SRP-9001 (marketed as ELEVIDYS®), which was originally approved by the FDA in June 2023 for the treatment of ambulatory pediatric patients aged 4 through 5 years with DMD with a confirmed mutation. In June 2024, the FDA granted approval of an expansion to the labeled indication for ELEVIDYS to include individuals with DMD with a confirmed mutation in the DMD gene who are at least 4 years of age, granting traditional approval for ambulatory patients and accelerated approval for non-ambulatory patients. Continued approval for non-ambulatory DMD patients may be contingent upon verification of clinical benefit in a confirmatory trial. There are additional investigational gene therapy programs in different stages of development to treat DMD. It is important to note that adeno-associated virus, or AAV-based gene replacement approaches deliver a significantly truncated dystrophin (micro-dystrophin) which we believe has the potential to limit the therapeutic efficacy of the approved and clinical stage AAV-based pipeline candidates. In addition, there are gene editing treatments that are in preclinical development. Exon skipping does not face some of the inherent challenges associated with gene therapy modalities, including:

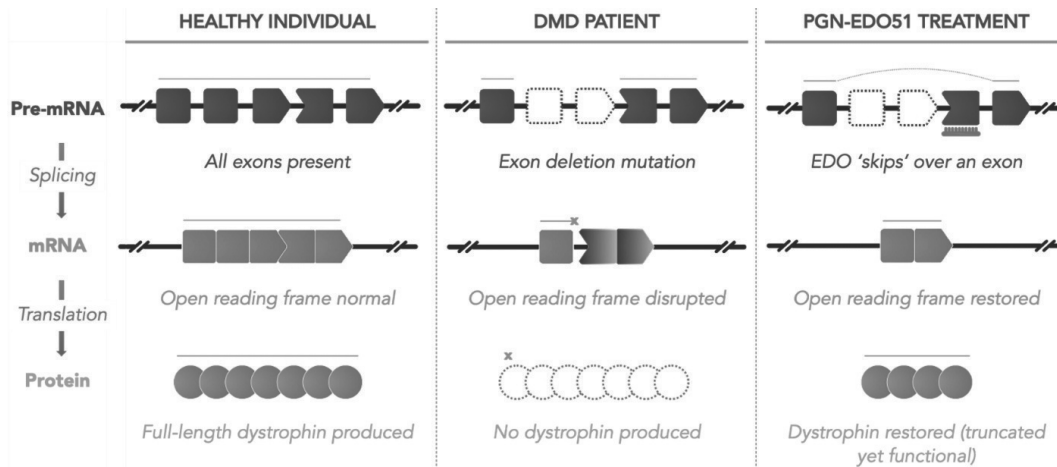
- Limited packaging size of AAV vectors, resulting in the need to employ truncated ‘micro-dystrophin’ genes with an unclear functional benefit, where >70% of the dystrophin gene is omitted, including regions that correspond to key structural and binding domains;
- Increased safety concerns with high-dose AAV-based gene therapies (e.g., complement activation);
- Immunogenicity of AAV, resulting in:
 - o Up to half of all patients possessing antibodies against the most commonly used recombinant AAV vector serotypes, precluding their eligibility for treatment;
 - o Production of anti-AAV antibodies in treated patients, resulting in an inability to re-dose; and
 - o Loss of gene copies over time as patients mature and their cells divide, reducing the durability of therapeutic effect;
- Complexity and challenges inherent to manufacturing of AAV-based therapies.

We are also aware of several companies targeting non-dystrophin mechanisms for the treatment of DMD.

We believe that an exon skipping approach aimed at producing functional, truncated dystrophin will be a cornerstone approach to effectively treat patients with DMD.

Our Approach

We are developing or evaluating product candidates for the treatment of DMD in which exon skipping PMOs are conjugated to our EDO peptide in order to enhance their delivery to muscle cells. Our initial product candidate is PGN-EDO51, an investigational EDO peptide-conjugated exon 51-skipping ASO with a proposed mechanism of action we believe to be identical to that of eteplirsen.



PGN-EDO51 is designed to facilitate the skipping of exon 51, allowing the synthesis of a shortened, but functional, dystrophin.

The key differentiator between PGN-EDO51 and other exon 51-skipping approaches is the greater exon skipping activity observed with PGN-EDO51 in HVs, in early data from DMD patients, and in preclinical models. We believe the higher levels of exon skipping observed with PGN-EDO51 in HVs and in early data from DMD patients when compared to publicly available data from other therapies is directly related to the potential of our EDO platform to drive superior cellular uptake and nuclear delivery of the PMO cargo therapeutic resulting in exon skipping of the defective dystrophin mRNA.

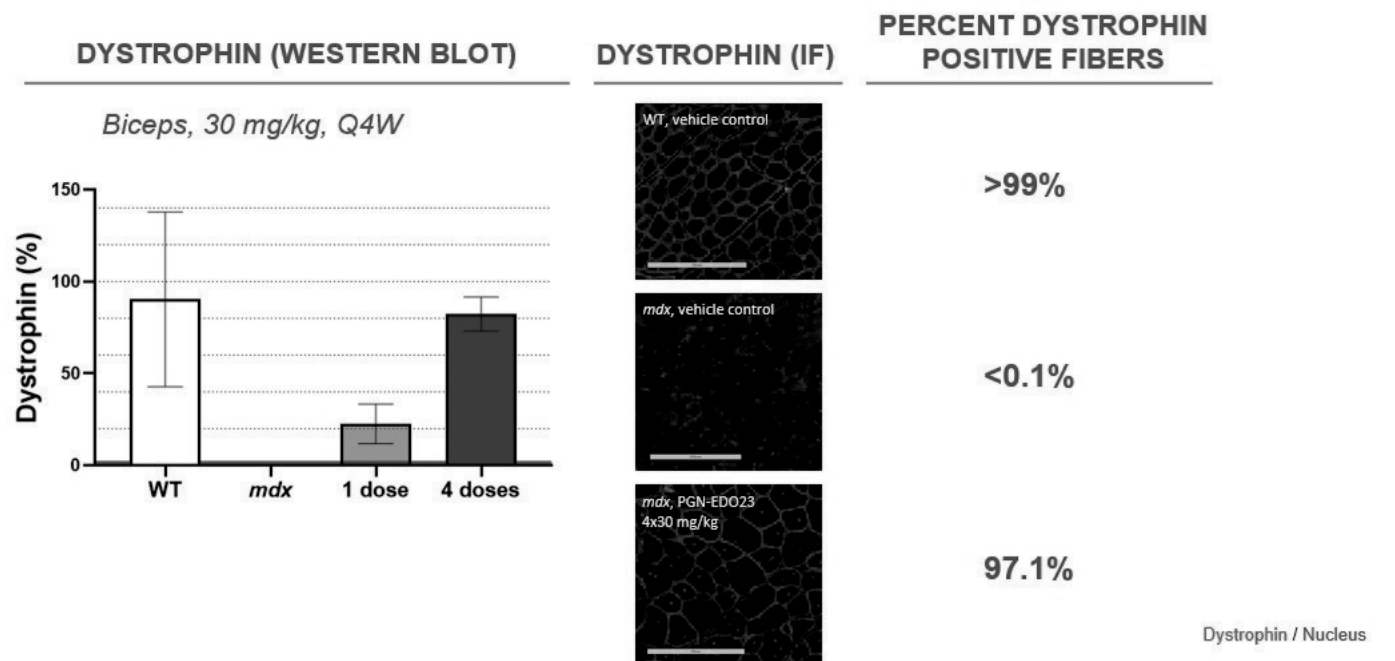
Our Preclinical Data

We have evaluated the pharmacology of PGN-EDO51 in a number of *in vitro* and *in vivo* preclinical studies and have observed robust activity in every model system evaluated.

We conducted a repeat-dose study where we dosed *mdx* mice with 30 mg/kg of PGN-EDO23, a murine analogue of PGN-EDO51, every four weeks, with up to four doses, with tissue collection and analysis four weeks following the final dose. In the biceps, dystrophin production was measured by western blot and was observed to reach a mean level of 82.2% in the same tissue after four doses in comparison to a level of 22.5% obtained after a single dose. We believe this marked increase of 3.7 times between the level of dystrophin obtained following one dose, and the level obtained following four doses supports the clinical potential of a once-every-four-week dosing regimen for PGN-EDO51 and serves to highlight our belief that dystrophin production is likely to increase with additional doses over a longer treatment period.

In addition, in this repeat dosing study in *mdx* mice, dystrophin protein localization and the percent dystrophin positive fibers, or PDPF, were evaluated by immunofluorescence microscopy. Importantly, this orthogonal assessment of dystrophin demonstrated that dystrophin protein was uniformly distributed across the skeletal muscle sarcolemma and found 97.1% of biceps muscle fibers were

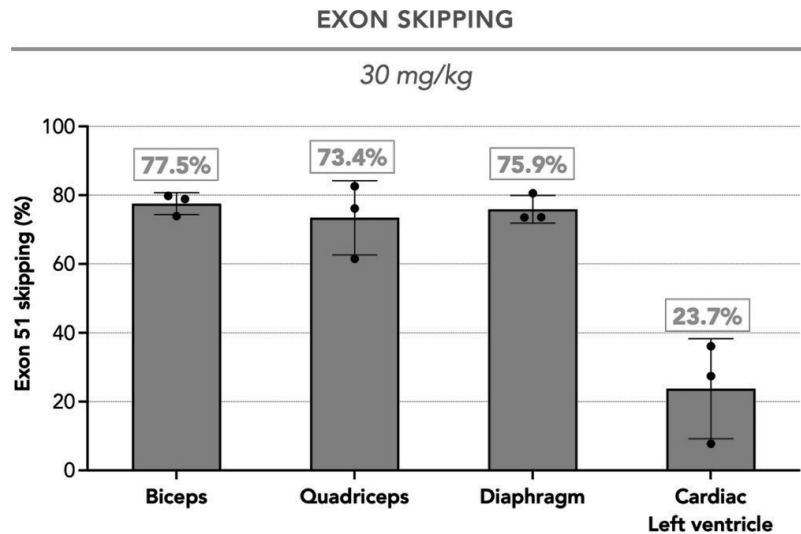
dystrophin positive following four doses of PGN-EDO23 administered once every four weeks, which was close to wild type, or *WT*, dystrophin levels (>99%).



Dystrophin levels and distribution in skeletal muscle with repeat dosing of PGN-EDO23 in *mdx* mice. *Dystrophin protein evaluation by western blot and immunofluorescence (IF). Graph is presented as mean ± SD; n = 4-5 per cohort; grey band is dystrophin LLOQ (2.5%).*

We have also conducted a number of studies in NHPs and have observed the robust *in vivo* activity of PGN-EDO51 in this higher order animal model. There is complete homology of the oligonucleotide binding site between the DMD gene in humans and the DMD gene in NHPs for an exon 51-skipping therapeutic, thus allowing the activity of our clinical candidate to be assessed in this species.

For example, following three bi-weekly doses of 30 mg/kg, we observed robust exon skipping activity for PGN-EDO51, with mean levels of greater than 70% obtained in key skeletal muscles following analysis by RT-PCR seven days after the final dose. In biceps, a mean exon 51 skipping level of 77.5% was obtained; and in quadriceps, 73.4%. We observed mean exon 51 skipping levels of over 20% in the left ventricle for PGN-EDO51, and 75.9% in the diaphragm, and we believe that these results highlight the potential of PGN-EDO51 to address the key cardio-respiratory morbidities affecting multiple organs observed in DMD.



Repeat dose administration of PGN-EDO51 in NHPs yielded high exon skipping rates in the key skeletal muscles, including the diaphragm, and in the cardiac left ventricle. Graph plotted as mean $\pm$ SD; $n = 3$ per group; study was not powered for statistical significance.

We have completed a number of Good Laboratory Practice, or GLP, studies that support a generally well-tolerated safety profile for PGN-EDO51, including repeat-dose NHP studies of PGN-EDO51. In one such study, we administered 11 doses of PGN-EDO51 intravenously to NHPs at 45 mg/kg over 60 minutes every 28 days over 39 weeks, and serum chemistry markers were assessed. Following the first administration, an elevation in serum creatinine was observed at day two; this elevation was completely resolved by day eight. Importantly, there were no adverse findings in the kidney even after 11 doses and there were no notable hematologic, cardiovascular or hepatic effects in this study. Additionally, following subsequent administrations, the day two elevations seen after the first dose were of lower magnitude. We believe these data support an acceptable tolerability profile for the ongoing CONNECT1 and CONNECT2 clinical studies.

Clinical Development

Phase 1 HV Study

In 2022, we completed a first-in-human, Phase 1, single-center, randomized, double-blind, placebo-controlled, SAD clinical trial to assess the target engagement (exon skipping), pharmacokinetics (oligonucleotide tissue concentration), safety and tolerability of PGN-EDO51 administered intravenously to 32 healthy adult male volunteers. Following administration, safety data were evaluated by a safety review committee prior to progressing to the next dose level. Volunteers were dosed with either 1, 5, 10 or 15 mg/kg of PGN-EDO51 or placebo. Oligonucleotide tissue concentration and exon skipping were assessed from needle biopsies of biceps muscle taken on days 10 and 28, with the latter being measured by a ddPCR assay.

A dose-dependent increase in mean exon skipping was observed in biceps.

- In the 10 mg/kg dose cohort, PGN-EDO51 exhibited mean exon skipping of 1.4% in biceps biopsies taken at day 28 ($n=6$).
- In the 15 mg/kg dose cohort, PGN-EDO51 exhibited mean exon skipping of 2.0% in biceps biopsies taken at day 28 ($n=6$).

A dose-dependent increase in PGN-EDO51 tissue concentration was observed in biceps.

- In the 10 mg/kg dose cohort, PGN-EDO51 exhibited mean oligonucleotide tissue concentrations of 11 nM in biceps biopsies taken at day 28 ($n=6$).
- In the 15 mg/kg dose cohort, PGN-EDO51 exhibited mean oligonucleotide tissue concentrations of 50 nM in biceps biopsies taken at day 28 ($n=6$).

We believe that the exon skipping data obtained from HVs in this clinical trial indicate the potential for clinically meaningful accumulation of exon 51-skipped transcripts and dystrophin in patient tissue with repeated doses of PGN-EDO51. Thus, based on these data, we anticipate that the exon skipping rates afforded by PGN-EDO51 when administered to patients have the potential to exceed the rates observed when administered to HVs. We believe the initial data from our CONNECT1 Phase 2 study, described below, further supports this potential.

The Phase 1 trial met its primary endpoint, providing evidence that PGN-EDO51 was observed to be generally well-tolerated at potentially clinically relevant dose levels. By way of example, at a dose of 10 mg/kg:

- All participants completed the study with no discontinuations;

- All related treatment-emergent adverse events, or TEAEs, including transient, reversible changes in kidney biomarkers, were assessed as mild and resolved without any intervention;
- Serum cystatin C, the recommended biomarker to assess renal function in DMD, did not change; and
- There was no evidence of hypomagnesemia.

At 15 mg/kg there was one non-life threatening serious adverse event, or SAE, related to changes in kidney biomarkers that were transient and reversible. This HV was admitted to the hospital for less than 24 hours, received hydration and then was re-admitted to the Phase 1 unit and completed the study. There were no clinical symptoms of acute kidney injury in any of the subjects. We also observed transient mild (Grade 1) hypomagnesemia in one participant and moderate (Grade 2) hypomagnesemia in one participant at the 15 mg/kg dose that did not require any intervention.

Under the Phase 1 protocol for PGN-EDO51, any non-life-threatening SAE was considered a dose-limiting toxicity, or DLT, however the study was not halted by the safety review committee, nor was it put on hold by Health Canada. In light of higher than anticipated oligonucleotide levels and exon skipping levels in muscle observed at 5 mg/kg and 10 mg/kg, we determined that further dose escalation in the Phase 1 study was not necessary.

CONNECT1 and CONNECT2 Phase 2 MAD Studies

The results from our Phase 1 HV clinical trial, together with the experience and expertise of our clinical development team and scientific advisory board, as well as learnings from previous clinical studies conducted in exon 51 skipping-amenable DMD patients, have guided the design, parameters and objectives of our planned Phase 2 clinical trials of PGN-EDO51 in DMD patients amenable to an exon 51-skipping approach.

The Phase 2 clinical development plan for PGN-EDO51 consists of two studies conducted in parallel; a smaller open-label MAD study, CONNECT1, is being conducted in Canada. A larger, randomized, double-blind placebo-controlled MAD study, CONNECT2, is open in the U.K., with plans to evaluate opening the study in other geographies subject to regulatory authorizations. In December 2024, we announced that we received a clinical hold notice from the FDA regarding our IND application to initiate the CONNECT2 study in the U.S. We are working with the FDA to address its questions regarding supportive data for the dosing levels planned for the patient population.

In the CONNECT1 study, PGN-EDO51 is being administered once every four weeks at 5 mg/kg and 10 mg/kg for 12 weeks. Dose escalation is based on data review by a data safety monitoring board, or DSMB. We are conducting muscle biopsies at baseline and initially, week 13, amended to week 16 for the 10 mg/kg cohort. In addition to assessing safety and tolerability, we are measuring exon skipping and dystrophin expression in CONNECT1. At the end of the CONNECT1 study period, participants have the option to enroll in the LTE phase of the study. We began dosing participants in our CONNECT1 study in early 2024 and in July 2024, we reported initial data from the 5 mg/kg starting dose cohort (n=3), as follows:

Exon Skipping. PGN-EDO51 produced mean exon skipping in biceps tissue of 2.15% at week 13 compared to baseline, measured by RT-PCR after four doses and three months of treatment. All participants demonstrated increased levels of exon skipping following treatment with PGN-EDO51, and we believe exon skipping will continue to increase with higher doses over a longer treatment period.

Dystrophin Production. PGN-EDO51 achieved a mean muscle-adjusted dystrophin level of 1.49% of normal (0.70% increase from baseline) and a mean absolute dystrophin level (by Western blot analysis) of 0.61% of normal (0.26% increase from baseline), in each case after four doses, measured at week 13. All participants demonstrated increased dystrophin production following treatment with PGN-EDO51. With a longer treatment period and higher doses of PGN-EDO51, we expect to see higher levels of exon skipped transcript potentially resulting in significant increases in dystrophin.

Muscle Concentration. Consistent with the observed levels of exon skipping and dystrophin, treatment with PGN-EDO51 resulted in ~30nM of oligonucleotide in the muscle.

As of January 23, 2025, all three participants in the 5 mg/kg cohort were continuing to be dosed with PGN-EDO51 at 5 mg/kg in the LTE phase of the clinical trial.

Based on learnings from the 5 mg/kg cohort, we have amended the CONNECT1 study protocol. The changes include adjusting the timing for the final biopsy from day 7 to day 28, as noted above, adjusting the Performance of Upper Limb, or PUL, test entry score from three to four for inclusion, and adjusting the eligible age group from eight years of age and older to six - 16 years of age. We also expanded the 10 mg/kg cohort from three to four participants.

In December 2024, we announced that the 10 mg/kg cohort of CONNECT1 was fully enrolled (n=4). As of January 23, 2025, a total of 17 doses had been administered at 10 mg/kg in the ongoing study. Based on the totality of data in both the 5 mg/kg cohort and the ongoing 10 mg/kg cohort in the CONNECT1 trial as of January 23, 2025, we continue to believe PGN-EDO51 has a favorable emerging safety profile. Magnesium levels in two of the participants in the 10 mg/kg cohort, who were previously reported as having asymptomatic hypomagnesemia, have returned to levels within normal limits with administration of ongoing low-dose oral magnesium supplementation. Dosing of one of these two participants was paused due to a reduction of his estimated glomerular filtration rate, or eGFR. This event did not meet the pre-specified criteria for a DLT. A subsequent nuclear scan indicated measured glomerular filtration rate was in the normal range. The participant's eGFR is improving and the investigator is evaluating for the resumption of dosing as this value returns to baseline levels. We are continuing to review the event and associated potential

confounding factors to better understand its manifestation. There have been no treatment-related SAEs, and all treatment-related adverse events have been mild. There was no sustained elevation in kidney biomarkers. There were also no cases of hypokalemia, anemia or thrombocytopenia. We expect to report clinical data from the 10 mg/kg cohort by the end of the third quarter of 2025.

We have received communication from Health Canada that dosing of participants in the 5 and 10 mg/kg cohorts may continue at their current dose levels. Health Canada has requested additional information from us to address its safety concerns before any further dose escalation or enrollment of any additional participants at the current dose levels. We are working with Health Canada to address its questions.

As noted above, we have opened the CONNECT2 study in the U.K. CONNECT2 will enroll approximately 20 ambulatory and non-ambulatory boys and young men living with DMD amenable to exon 51 skipping, who are at least six years of age. Participants will receive seven doses of either PGN-EDO51 or placebo at approximately four-week intervals for 24 weeks. Based on the data from CONNECT1, including PGN-EDO51's favorable emerging safety profile to date, we have optimized the design of the CONNECT2 trial.

The starting dose of CONNECT2 was amended in the U.K. to be 10 mg/kg with escalation to potentially higher doses (if needed). Dose escalation will be determined based on data review by the DSMB. We will conduct muscle biopsies at baseline and at week 28. We will assess safety, tolerability, exon skipping, dystrophin production and functional outcome measures in this study. As noted above, in December 2024, we announced that we received a clinical hold notice from the FDA regarding our IND application to initiate the CONNECT2 study in the U.S. We are working with the FDA to address its questions regarding supportive data for the dosing levels planned for the patient population. In parallel, we are evaluating opening CONNECT2 in other geographies outside of the U.S., subject to regulatory authorizations.

The CONNECT2 study, together with data from the CONNECT1 study, is intended to support a potential accelerated approval pathway for PGN-EDO51 with the FDA, subject to regulatory authority feedback.

PGN-EDODM1

Overview

We are developing PGN-EDODM1, an EDO peptide-conjugated PMO, for the treatment of DM1, a debilitating genetic disease with no approved therapies. PGN-EDODM1 leverages the same EDO peptide as PGN-EDO51 to deliver a PMO into muscle cells that binds to the pathogenic CUG trinucleotide repeat expansion present in the *DMPK* mRNA, thus reducing the ability of these trinucleotide repeats to sequester RNA binding proteins like MBNL1, a critical RNA processing protein. This approach, which is not designed to knock down *DMPK*, directly addresses the underlying genetic defect of this disease, and we have observed robust levels of activity in preclinical models with both long and short CTG repeats. In DM1 patient cells, we observed that treatment with PGN-EDODM1 led to a reduction in toxic nuclear foci, and liberated bound MBNL1 which mediated robust correction of mis-splicing. In preclinical studies in the mouse HSA^{LR} DM1 model, multiple monthly doses of PGN-EDODM1 corrected 99% of transcript mis-splicing and myotonia.

On February 24, 2025, we reported initial data from our FREEDOM Phase 1, randomized, placebo-controlled SAD clinical trial of PGN-EDODM1 in DM1 patients. We believe these data demonstrate that PGN-EDODM1 has a favorable emerging safety profile. Robust splicing correction in a dose-dependent manner was observed in the 5 and 10 mg/kg dose cohorts at day 28 after treatment with a single dose of PGN-EDODM1. The 15 mg/kg cohort is currently enrolling participants and we have begun dosing at this level. We anticipate reporting data from this cohort in the second half of 2025. We also initiated our FREEDOM2 Phase 2 randomized, double blind, placebo-controlled MAD study in DM1 patients in the U.K. and Canada in the second half of 2024. We are currently dosing participants in the 5 mg/kg dose cohort of this study and we expect to report data from this cohort in the first quarter of 2026.

The FDA has granted both orphan drug designation and Fast Track designation for PGN-EDODM1 for the treatment of DM1.

Disease Background and Prevalence

DM1 is a monogenic, autosomal dominant, progressive disorder that primarily affects skeletal, cardiac and smooth muscles, with central nervous system, or CNS, symptoms also being evident. Globally, the prevalence of DM1 is estimated to be 1 in 8,000 people, with approximately 40,000 patients in the U.S., 75,000 patients in Europe and 15,000 patients in Japan. However, under- and misdiagnosis is believed to be widespread, and genetic screening studies for *DMPK* triplet repeats have suggested that the prevalence of DM1 may be as high as 1 in 2,100 people.

DM1 patients can suffer from various manifestations of disease including myotonia, or a temporary rigidity due to the inability to relax muscles, muscle weakness, cardiac abnormalities, respiratory problems, fatigue, gastrointestinal complications, early cataracts, and cognitive and behavioral impairments. For patients with more severe forms of DM1, life expectancy is reduced due to increased mortality rates resulting from pulmonary and cardiac complications.

The broad spectrum of pathologies associated with DM1 arise due to genetic changes in the *DMPK* gene. Specifically, DM1 is caused by an expansion in the number of CTG triplet repeats that are present in the non-coding region of the *DMPK* gene, and following transcription this mutant *DMPK* gene yields an mRNA product with an expanded CUG repeat region. Healthy, asymptomatic individuals possess between 5 and 37 such repeats, but in DM1 patients the number of repeats can be in the thousands. These highly repetitive sequences form stable hairpin structures in the nucleus of cells and sequester critical RNA splicing proteins, such as MBNL1, leading to the formation of nuclear foci. The sequestration of MBNL1 prevents this key protein from performing its

normal function of processing RNA molecules before they are exported from the nucleus, leading to downstream mis-splicing events in a number of other transcripts. The mis-splicing of these transcripts results in the dysregulation of a broad set of downstream proteins, which in turn leads to in the multi-systemic pathologies that are associated with DM1, which include:

- **Musculoskeletal:** Myotonia (a temporary inability to relax a muscle after contraction), muscle weakness & wasting.
- **Cardiac:** Conduction defects.
- **Respiratory:** Breathing difficulties, sleep apnea.
- **Gastrointestinal:** Dysphagia (difficulty swallowing), constipation, Irritable Bowel Syndrome.
- **CNS:** Cognitive impairments, behavioral / psychological disorders, excessive daytime sleepiness.
- **Vision:** Early-onset cataracts, retinal damage.
- **Endocrine:** Thyroid dysfunction, diabetes.
- **Other pathologies:** Skin, immune system and reproductive pathologies, increased cancer risk.

There is a general correlation between the number of CTG repeats in the aberrant *DMPK* gene and the severity of disease. Individuals with 50 to 150 repeats are prone to development of mild myotonia and cataracts, but typically have a normal lifespan. Individuals with up to approximately 1,000 repeats typically have muscle weakness and cardiac arrhythmia, with an average lifespan of 48 to 55 years. The most serious cases of DM1 are generally observed in individuals with more than 1,000 repeats, and these patients are likely to also suffer from respiratory defects and intellectual disability, with a shortened lifespan of approximately 45 years. Genetic anticipation is also observed, whereby the age of onset decreases in subsequent generations due to expansion of the CTG repeat between generations.

Current Approaches and Limitations

There are no approved therapies to treat DM1, with current standards of care being medicines that are used off-label for symptom management. Previously, a phosphorothioate ASO designed to cause degradation of the *DMPK* transcript was clinically assessed as a therapeutic for DM1. However, this therapeutic approach was restricted by the inefficiency of ASO delivery into target tissues and cells, thus limiting the effective clinical translation of this product candidate.

There are several clinical-stage approaches leveraging antibody-oligonucleotide conjugate, or AOC, technologies, that are currently in development for the treatment of DM1. These approaches utilize mAbs and Fabs that target the transferrin receptor 1, or TfR1, in order to deliver cargo oligonucleotides that are designed to knockdown or degrade *DMPK*. Such knockdown or degradation approaches cannot differentiate between expanded and non-expanded transcripts. In contrast to knockdown or degradation of overall *DMPK* levels, our approach is more targeted as PGN-EDODM1 is designed to disrupt the binding of MBNL1 to the *DMPK* transcript. This approach maintains overall *DMPK* levels and thereby averts any potential for haploinsufficiency, a condition where a copy of the gene is deleted or mutated and the remaining copy is unable to produce sufficient protein for normal function. Furthermore, the correlation between the level of *DMPK* knockdown and the level of splicing correction required for therapeutic benefit is currently unclear, a consideration that may confound clinical development of these approaches. Therefore, we believe that PGN-EDODM1 is differentiated relative to the *DMPK* knockdown approaches in development for DM1 given its mechanism of action that is intended to bind *DMPK*, allowing release of MBNL1 to restore splicing and downstream functional effects. In addition, in preclinical studies and early clinical studies, the EDO platform has shown successful delivery of therapeutic PMOs to the nucleus, which we believe is critical to drive the anticipated therapeutic benefit of PGN-EDODM1.

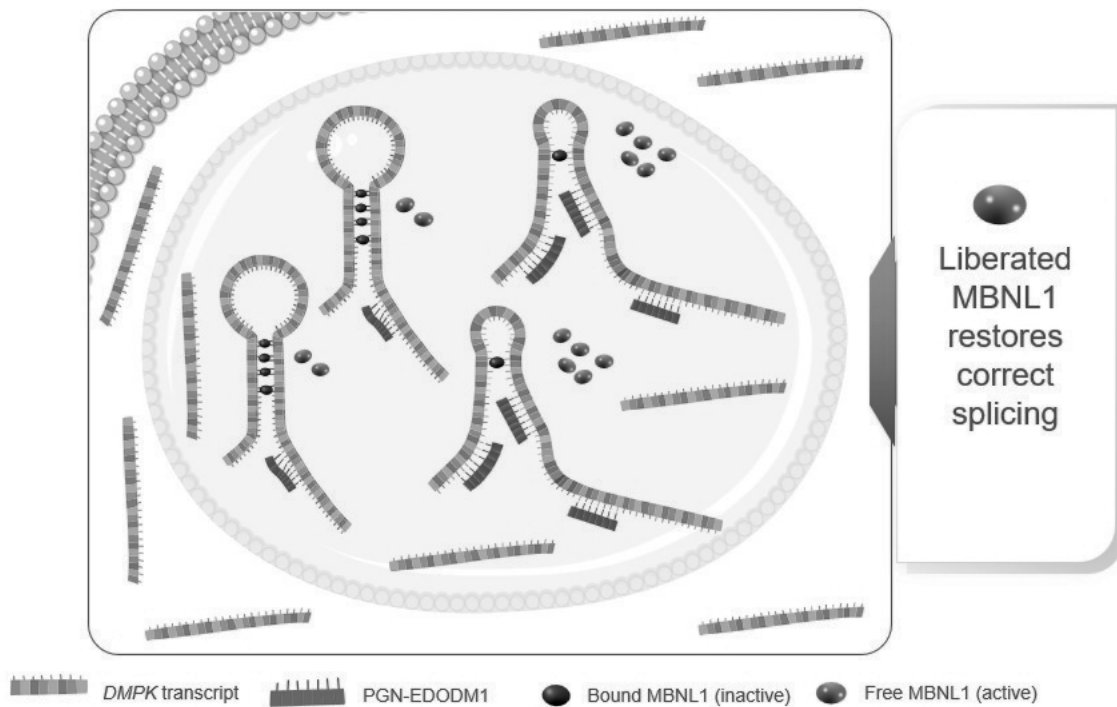
We are also aware of another CPP approach conjugated to a PMO that is designed to block the CUG repeats in the *DMPK* transcript that is being evaluated in a Phase 2 study in patients with DM1.

Our Approach

Our product candidate for the treatment of DM1, PGN-EDODM1, consists of our lead EDO CPP conjugated to an ASO that binds to the pathogenic CUG repeat expansion in the *DMPK* mRNA. We are employing the same EDO peptide in PGN-EDO51 and PGN-EDODM1. PGN-EDODM1 is designed to directly address the deleterious effects of genetic alteration in DM1, specifically the sequestration of MBNL1 due to the high number of CUG repeat expansion in the *DMPK* transcript.

We believe that this innovative therapeutic approach has considerable advantages over oligonucleotide modalities that rely on knockdown or degradation of the *DMPK* transcript. PGN-EDODM1 disrupts the binding between the CUG repeat expansion and MBNL1, an approach which we believe will allow the *DMPK* transcript to continue performing its normal function within the cell,

while also liberating MBNL1 to correct downstream mis-splicing events. We believe that this therapeutic strategy positions us to potentially provide clinically meaningful benefits for DM1 patients while mitigating the risk of potential deleterious outcomes.



PGN-EDODM1 is designed to bind to the CUG repeats in *DMPK* RNA and liberate MBNL1 to restore physiological splicing, in contrast to modalities that indiscriminately target both normal and pathogenic *DMPK* for degradation.

Preclinical Data

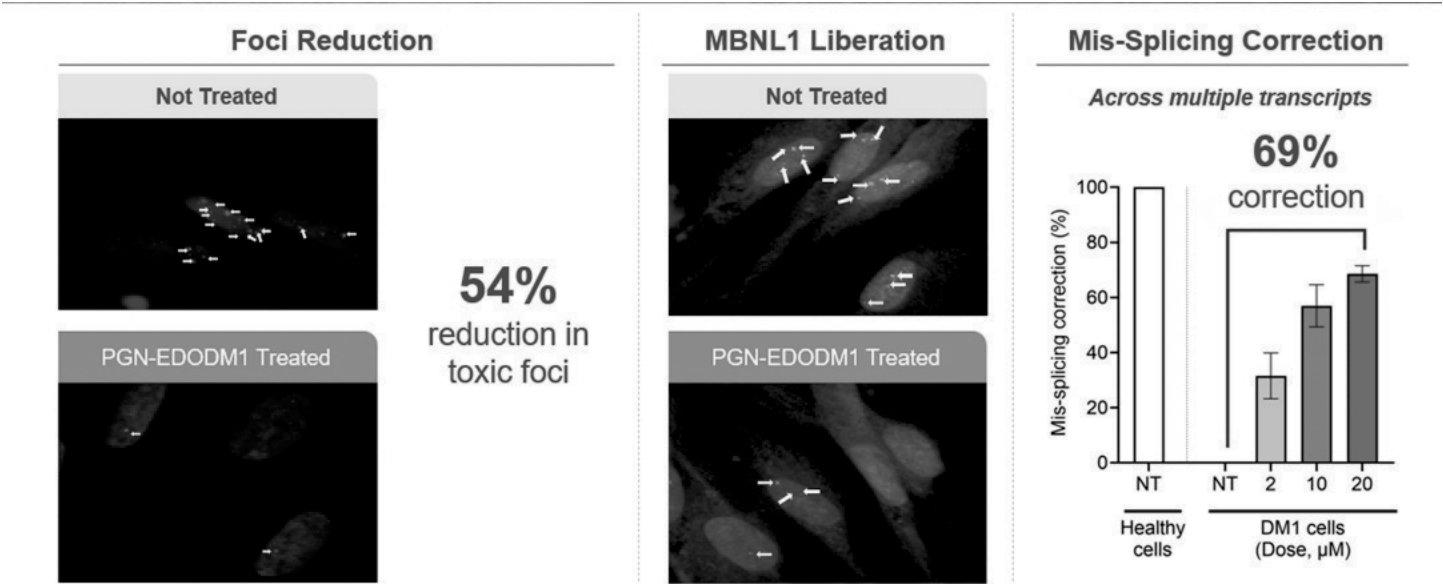
In an *in vitro* study utilizing DM1 patient cells with approximately 2,600 CTG repeats in the *DMPK* gene, we observed a robust reduction in nuclear foci, liberation of MBNL1 from foci and the correction of downstream transcript mis-splicing pathologies. In this study, immortalized myoblasts from a DM1 patient were differentiated for four days, and then treated for 24 hours with PGN-EDODM1 at a range of concentrations from 0 μ M to 20 μ M. Myoblasts from a healthy individual were utilized as a control, and the unconjugated PMO was also assessed at a concentration of 20 μ M in this study in order to demonstrate the critical role that our EDO platform plays in driving efficient cell uptake of this therapeutic cargo.

A characteristic feature of DM1 is the accumulation of nuclear foci, or myonuclear aggregates of *DMPK* mRNA bearing the pathogenic CUG repeat expansion. These foci sequester MBNL1, a critical modulator of transcript splicing, and thus play a key role in the downstream spliceopathies that are observed in this multi-systemic disorder. We assessed the impact of PGN-EDODM1 treatment on the presence of nuclear foci in DM1 cells through visualization with fluorescence *in situ* hybridization, or FISH, and immunofluorescence co-staining, and we observed that treatment led to a robust mean reduction of 54% in the number of these toxic aggregates. In contrast, treatment with the unconjugated PMO cargo did not yield a reduction in nuclear foci, an observation which we believe supports the potential utility of our EDO platform in driving the successful delivery of therapeutic agents to their nuclear site of action.

In this same *in vitro* study, we also assessed the impact of PGN-EDODM1 treatment on the sequestration of MBNL1. Following treatment and visualization, we observed a mean reduction in the amount of foci-bound MBNL1, indicating that this critical splicing factor is liberated upon treatment with our DM1 product candidate. We believe these results provide additional support for the proposed mechanism of action of PGN-EDODM1, suggesting that – once delivered to the cell nucleus – our therapeutic cargo may bind to the CUG repeat expansion present in the *DMPK* transcript, resulting in a reduction in the number of nuclear foci and the liberation of MBNL1.

Furthermore, treatment of DM1 patient cells with PGN-EDODM1 led to robust correction of downstream mis-spliced transcripts associated with key disease pathologies in a dose-dependent fashion. At the highest dose assessed, 20 μ M, PGN-EDODM1 treatment resulted in robust mis-splicing correction, resulting in mean exon inclusion or exclusion rates of approximately 70% of healthy control levels in these transcripts. We believe this observation supports our therapeutic hypothesis that treatment with PGN-

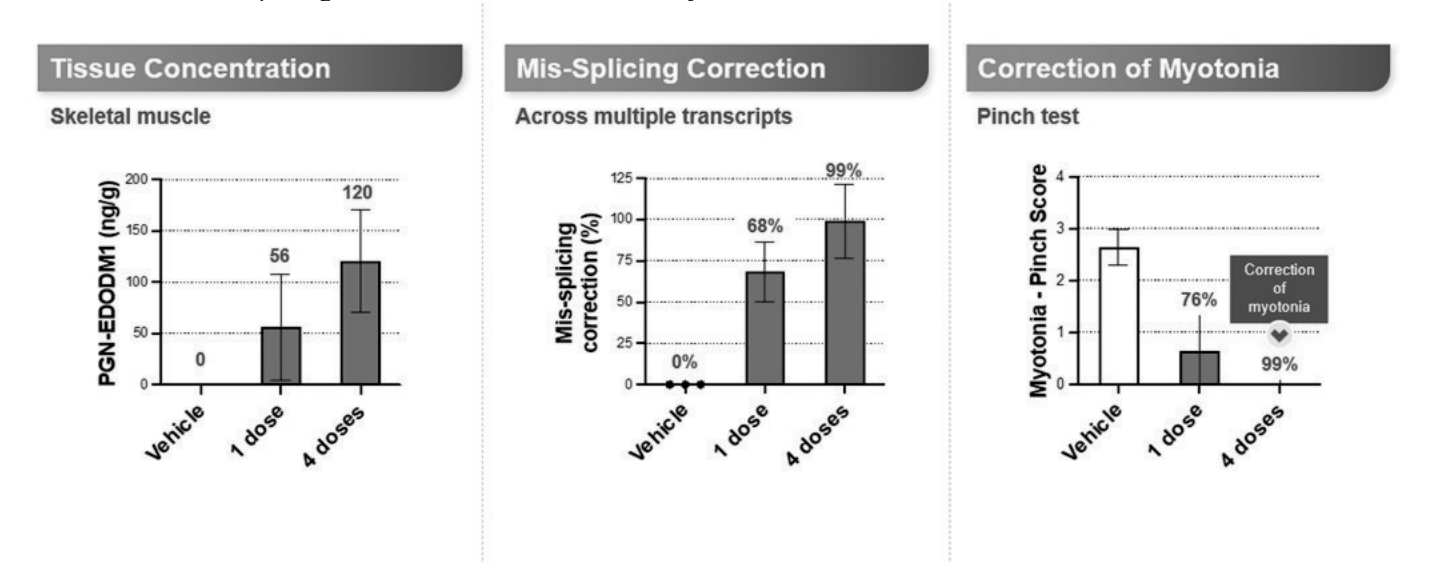
EDODM1 may restore the altered global spliceopathy profiles seen in DM1 patients, thus ameliorating the key pathologies that are the hallmark of this devastating disease.



PGN-EDODM1 Reduced Pathogenic Nuclear Foci, Liberated MBNL1 and Corrected Mis-Splicing in Patient Cells with Long CUG Repeats. *Immortalized myoblasts from healthy individuals or DM1 patients were cultured then differentiated for four days into myotubes. Treatment with peptide-PMO conjugates at concentrations given. Cells were harvested for analysis 24h after treatment. RNA isolation, RT-PCR and capillary electrophoresis (QIAxcel) analysis were performed. Visualization with FISH and immunofluorescence microscopy. Mean ± SD; n = 5 per group.*

Building on the encouraging positive data from our *in vitro* studies, we utilized the HSA^{LR} mouse model of DM1 to assess the activity of PGN-EDODM1. This transgenic mouse model contains between 220 and 250 CTG trinucleotide repeats in the inserted *human skeletal actin*, or *HSA*, gene, and exhibits molecular and functional pathologies that are very similar to those seen in human DM1 patients. The CUG repeat expansion present in the HSA^{LR} mouse model, and the subsequent sequestration of MBNL1, leads to downstream defects in the normal mRNA splicing patterns for a number of transcripts, resulting in aberrant inclusions or exclusions of exons. Sequestration of MBNL1 in the HSA^{LR} mouse model causes mis-splicing of multiple RNAs. This mis-splicing causes the mice to exhibit myotonia, effectively recapitulating the classic symptom of disease that is observed in DM1 patients.

We dosed HSA^{LR} mice with one or four doses of PGN-EDODM1, with four-week intervals between doses. Skeletal muscle tissues were collected four weeks post-final dose. Skeletal muscle tissue concentration was measured by fluorescent based HPLC method. Following multiple doses of PGN-EDODM1 at 30 mg/kg given once every four weeks, PGN-EDODM1 produced a mean 99% correction of mis-splicing and a mean 99% correction of myotonia.



PGN-EDODM1 demonstrated enhanced efficacy in terms of splicing correction and improvement in myotonia after repeat doses vs. single doses in preclinical study in HSA^{LR} mice HSA^{LR} mice. *Skeletal muscle tissue concentration was measured by fluorescent based HPLC method. Graph is presented as mean $\pm$ SD; n = 8-12 per cohort. Mis-splicing analysis considers multiple transcripts. Graph is presented as mean $\pm$ SD; n = 8-12 per cohort per transcript. Action myotonia evaluation (pinch test) was performed four weeks post-final dose. Grade 3 = Clear sign of myotonia strong AND reproducible, Grade 2 = Clear sign of myotonia, strong OR reproducible, Grade 1 = Clear sign of myotonia but non reproducible, Grade 0 = No sign of myotonia. Graph is presented as mean $\pm$ SD; n = 12-43 per cohort.*

We have completed a number of GLP studies that support a generally well-tolerated safety profile for PGN-EDODM1, including repeat-dose NHP studies of PGN-EDODM1. In one such study, we administered 11 doses of PGN-EDODM1 intravenously to NHPs, 10 of which were at 45 mg/kg, over 60 minutes every 28 days over 39 weeks, and serum chemistry markers were assessed. Following the first administration, an elevation in serum creatinine was observed at day two; this elevation was completely resolved by day eight. Following repeat-dose administrations of 45 mg/kg, the transient elevations in creatinine were of comparable magnitude, i.e., did not worsen. Importantly, there were no adverse findings in the kidney even after 11 doses and there were no notable hematologic, cardiovascular or hepatic effects in this study. We believe these data support an acceptable tolerability profile for the ongoing FREEDOM and FREEDOM2 clinical studies.

Clinical Development

Our clinical development program for PGN-EDODM1 includes two studies, FREEDOM, a multinational, randomized, double-blind, placebo-controlled Phase 1 SAD study, and FREEDOM2, a multinational, randomized, double blind, placebo-controlled Phase 2 MAD study. In the FREEDOM study, we intend to enroll up to approximately 32 adult participants with DM1 in multiple geographies including the U.S., U.K. and Canada, to evaluate the safety and tolerability of PGN-EDODM1. Per the protocol, PGN-EDODM1 was administered at starting doses of 5 mg/kg and 10 mg/kg with subsequent dose escalation to 15 mg/kg, and potentially in the future to 20 mg/kg, based upon evaluation by a DSMB of safety data from the prior dose cohort(s). We are conducting muscle biopsies at baseline, at day 28 and at week 16. In addition to safety and tolerability, we are assessing oligonucleotide muscle concentrations, splicing correction and functional outcome measures at day 28 and at week 16 following a single dose of PGN-EDODM1.

On February 24, 2025, we reported initial data from the 5 mg/kg and 10 mg/kg dose cohorts of the FREEDOM study. We believe PGN-EDODM1 has a favorable emerging safety profile. Through the data cutoff date of December 3, 2024, PGN-EDODM1 was observed to be generally well-tolerated, with most TEAEs being mild or moderate in severity. There were three SAEs, one of which was related to study drug (abdominal pain, 10 mg/kg) that was potentially confounded by use of a prohibited, off-label drug taken on the morning of PGN-EDODM1 dosing. Other SAEs included appendicitis (5 mg/kg) and right anterior tibial artery pseudoaneurysm (10 mg/kg; in connection with biopsy procedure). Four participants experienced seven study drug related TEAEs, as follows: nausea (n=2); vomiting (n=1); dizziness (n=1); headache (n=1); feeling hot (n=1); abdominal pain (n=1). There were no adverse events related to electrolytes or renal biomarkers.

Muscle Tissue Concentration. Treatment with a single dose of PGN-EDODM1 resulted in a mean 13.7 ng/g and 44.1 ng/g of PGN-EDODM1 in the muscle at 5 mg/kg (n=6) and 10 mg/kg (n=5)¹, respectively, at day 28 post-dosing, which is a greater than dose proportional increase in muscle concentration, which correlates with robust and dose-dependent splicing correction.

Splicing Correction. Following treatment with a single dose of PGN-EDODM1, a dose-dependent mean splicing correction from evaluable participants^{1,2} of 12.3% and 29.1% at 5 mg/kg (n=6) and 10 mg/kg (n=4), respectively, as measured by the 22-gene panel³, was observed at day 28 post-dosing.

Functional Outcomes.

10-Meter Walk Run Test/Myotonia (vHOT middle finger): While single-dose studies have not demonstrated improved functional outcomes in DM1 patients, we collected data from the 5 and 10 mg/kg cohorts that we believe showed positive early trends in some functional outcome measures. We believe robust splicing correction with PGN-EDODM1 has the potential to lead to meaningful functional improvements with repeat dosing over time.

1. One participant's biopsy was not collected at day 28 due to pseudoaneurysm in connection with the biopsy procedure.
2. One participant's sample at day 28 showed a splicing index outside the pre-specified assay range at baseline and day 28 (no detectable mis-splicing) and was excluded from the analysis.
3. Provenzano et al., The Splice Index as a prognostic biomarker of strength and function in myotonic dystrophy type 1, *J Clin. Invest.* 2025.

We expect to report data from the 15 mg/kg cohort of the FREEDOM study in the second half of 2025.

The safety data from the initial cohorts of the FREEDOM trial has informed the design of FREEDOM2 trial, which is currently open in Canada and the U.K. We also plan to open the FREEDOM2 study in other geographies, including the U.S., subject to regulatory authorizations. In the FREEDOM2 study, we intend to enroll approximately 24 adult participants with DM1 to evaluate the safety and tolerability of PGN-EDODM1. Per the protocol, PGN-EDODM1 is being administered at the starting dose of 5 mg/kg and will subsequently increase to 10 mg/kg and potentially 20 mg/kg, based upon evaluation by a DSMB of safety data from the prior dose cohort(s). Dosing will be administered every four weeks for a period of twelve weeks. We intend to conduct muscle biopsies at baseline and at week 16. In addition to safety and tolerability, we plan to assess oligonucleotide muscle concentrations, splicing

correction and functional outcome measures at week 16 following multiple doses of PGN-EDODM1. We expect to report data from the 5 mg/kg cohort of the FREEDOM2 study in the first quarter of 2026.

Based on the favorable emerging safety profile and robust initial splicing data from FREEDOM, we believe that PGN-EDODM1 has the potential to be disease-modifying and could improve outcomes for patients living with DM1.

Expanding the Application and Scope of Our EDO Platform

Additional DMD Patient Populations

We are also developing EDO therapeutics for additional DMD patient populations, including exon 53, 45 and 44. These programs utilize the same EDO CPP as PGN-EDO51. We plan to leverage significant learnings garnered from the preclinical and clinical development of PGN-EDO51 to advance one or more therapeutic candidates for additional DMD patient populations.

New Indications with PMO Therapeutics

In the future, we intend to apply our deep understanding of our EDO platform and PMO therapeutics to the development of additional product candidates in other indications. Based on extensive preclinical and early clinical data we have generated, we believe that the ability of our EDO peptides to deliver exon skipping and RNA blocking therapeutics to muscle cells and other target tissues positions us to develop additional product candidates in other neuromuscular indications as well as in potentially neurologic indications.

New Cargos

We believe that our EDO technology has the potential to facilitate the delivery of multiple types of oligonucleotide therapeutics. To date, our efforts have primarily focused on the delivery of PMOs, but we also intend to pursue the expansion of our cargo scope to other nucleic acid species.

New Peptide Technologies

We intend to further establish our expertise and competitive position in the field of oligonucleotide delivery through the ongoing research and development of new peptides. In connection with these efforts, we intend to leverage our deep expertise in this field to design new peptides that target specific tissue types, and to seek to further optimize the tissue and cellular delivery of our EDO platform.

Manufacturing

Our manufacturing process is modular in nature. The peptide and oligonucleotide components are assembled using readily available building blocks and are subsequently conjugated using well-established methodologies. This process is fully synthetic and does not rely on microbial fermentation, thus substantially reducing the risk of introducing microbial DNA or protein into our product candidates. Furthermore, our manufacturing process is scalable and easily characterizable – attributes that we intend to leverage to support the rapid development and clinical translation of our EDO conjugate therapeutics. We have produced, manufactured and released multiple batches under current Good Manufacturing Practice, or cGMP, and have successfully utilized this material in several clinical trials, including a completed Phase 1 HV study and ongoing Phase 1 and Phase 2 studies in patients.

We do not own or operate manufacturing facilities, and currently rely on third-party contract development manufacturing organizations, or CDMOs, for the CPP, linker and oligonucleotide components that comprise our EDOs, and for the conjugation of our product candidates as well as for the manufacturing of the finished dosage form (sterile injectable drug product). We anticipate that we will continue to utilize third-party CDMOs and suppliers to support our ongoing and future preclinical, clinical and commercial activities, and our intention is to build this network of organizations as we scale our manufacturing requirements. Long-term, we may also decide to establish internal manufacturing of our drugs or selected intermediates.

We believe that there are multiple sources for all raw materials employed in the manufacturing of our EDO therapeutics, and we believe that several CDMOs are able to assemble the peptide intermediate, the oligonucleotide intermediate and the final API.

There are extensive regulations that govern the manufacturing of pharmaceutical products, and the third-party manufacturing organizations we work with are required to adhere to these regulations. Our CDMOs are required to manufacture our product candidates under cGMP requirements, alongside other applicable laws and regulations.

Competition

The biopharmaceutical industry is characterized by the rapid evolution and development of new technologies, leading to an environment that is intensely competitive in nature and thus supports the robust protection and defense of intellectual property. Any EDO product candidates that we successfully develop and commercialize will compete both with existing therapeutics, and with new approaches that may arise in the future. While we believe that our unique EDO platform and extensive expertise in oligonucleotide delivery may provide us with a differentiated position in the neuromuscular and neurologic spaces, such competing technologies may

arise from many different sources, including large biopharmaceutical organizations, specialty pharmaceutical and biotechnology companies, academic institutions, government agencies, and public and private research organizations.

We expect to face competition from existing products and product candidates in development for each of our programs. Currently, patients with DMD are treated with corticosteroids to manage the inflammatory component of the disease. EMFLAZA® (deflazacort) is an FDA-approved corticosteroid marketed by PTC Therapeutics, Inc., or PTC. Individuals with DMD also use prednisone or prednisolone off-label. In addition, there are several FDA-approved exon skipping drugs: EXONDYS 51 and VYONDYS 53® (golodirsen), which are naked PMOs approved for the treatment of DMD patients amenable to exon 51 and exon 53 skipping, respectively, marketed by Sarepta; and VILTEPSO® (viltolarsen), a naked PMO approved for the treatment of DMD patients amenable to exon 53 skipping, which is marketed in the U.S. by NS Pharma, Inc. Notably, it was reported in May 2024 that the Phase 3, confirmatory study of VILTEPSO failed to meet the primary endpoint, Time to Stand from Supine, measured as velocity rise per second. Companies focused on developing treatments for DMD that target increased dystrophin expression, as our DMD program does, include Dyne Therapeutics, Inc., or Dyne, with DYNE-251, an antibody-conjugated PMO that targets exon 51 skipping in a Phase 1/2 clinical trial; BioMarin Pharmaceutical Inc., or BioMarin, with BMN-351, a phosphorothioate oligonucleotide that targets exon 51 skipping currently in preclinical development; and Wave Life Sciences Ltd., or Wave, with WVE-N531, a stereopure oligonucleotide in a Phase 1/2 clinical trial for patients amenable to exon 53 skipping. In November 2024, Sarepta announced it was discontinuing development of SRP-5051 (vesleteplirsen), a peptide-linked PMO for patients amenable to exon 51 skipping, based on the risk-benefit of the program, including some patients experiencing hypomagnesemia even after treatment discontinued, feedback from the FDA, and the evolving therapeutic landscape for DMD.

In addition, several companies are developing gene therapies to treat DMD. These include Sarepta's ELEVIDYS which was approved in June 2023 for treatment of ambulatory pediatric patients aged 4 through 5 years with DMD with a confirmed mutation in the DMD gene. In June 2024, the FDA granted approval of an expansion to the labeled indication for ELEVIDYS to include individuals with DMD with a confirmed mutation in the DMD gene who are at least 4 years of age, granting traditional approval for ambulatory patients and accelerated approval for non-ambulatory patients. Continued approval for non-ambulatory DMD patients may be contingent upon verification of clinical benefit in a confirmatory trial. In addition, several other companies are developing investigational gene therapies to treat DMD, including Solid Biosciences Inc.'s SGT-003 and REGENXBIO Inc.'s RGX-202, currently in Phase 1 and Phase 2 clinical development, respectively. Gene editing treatments that are in preclinical development are also being pursued by Vertex Pharmaceuticals, Inc., or Vertex, and Sarepta.

We are also aware of several companies targeting non-dystrophin mechanisms for the treatment of DMD, including Edgewise Therapeutics, Inc., or Edgewise, with EDG-5506, a muscle stabilizer that is currently in clinical development and Italfarmaco S.p.A., with Duvyzat™ (givinostat), an oral histone deacetylase, or HDAC, inhibitor, that reduces fibrosis in patients with DMD that was approved by the FDA in March of 2024 for the treatment of DMD in patients six years of age and older, and is under review by the EMA.

For DM1, there are currently no approved therapies to treat the underlying cause of the disease. Product candidates currently in clinical development to treat DM1 include several approaches that target *DMPK* RNA. These include AOC 1001, an antibody linked siRNA in Phase 3 clinical development by Avidity Biosciences, Inc., or Avidity; DYNE-101, an antibody conjugated antisense oligonucleotide in Phase 1/2 clinical development by Dyne; VX-670, a peptide conjugated PMO in Phase 2 by Entrada Therapeutics, Inc., or Entrada, and Vertex; and ARO-DM1, a conjugated siRNA in Phase 1/2 clinical development by Arrowhead Pharmaceuticals, Inc., or Arrowhead, and Sarepta. There are additional approaches under development such as ATX-01, a micro RNA that modulates the expression of MBNL1 by Arthex Biotech S.L. that is in Phase 1 development. Another small molecule, tideglusib, which is a GSK3-β inhibitor is in clinical development by AMO Pharma Ltd., or AMO, for DM1.

Several gene editing and gene delivery treatments are in discovery or preclinical development by Vertex and Kate Therapeutics Inc. (recently acquired by Novartis); Design Therapeutics, Inc., or Design, is developing an approach to prevent formation of CUG hairpins; Expansion Therapeutics, Inc., or Expansion, and Arrakis Therapeutics, or Arrakis, are developing an approach utilizing the interaction of small molecules with RNA in preclinical development; and therapeutics based on biomolecular condensate biology are in preclinical development by Dewpoint Therapeutics, Inc., or Dewpoint, and Pfizer.

We will also compete more generally with other companies developing alternative scientific and technological approaches, including companies working to develop conjugates with oligonucleotides for extra-hepatic delivery, including Alnylam Pharmaceuticals, Inc., or Alnylam, Aro Biotherapeutics Co., or Aro, Arrowhead, Avidity, Dicerna Pharmaceuticals, Inc. (acquired by Novo Nordisk), or Dicerna, Dyne, Entrada, Ionis Pharmaceuticals, Inc., or Ionis, NeuBase Therapeutics, Inc., or NeuBase, PYC Therapeutics Limited, or PYC, and Sarepta, as well as gene therapy and gene editing approaches.

Many of the companies which we compete with or may compete with in the future 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. Accordingly, our competitors may be more successful than us in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining approval for treatments and achieving widespread market acceptance, rendering our treatments obsolete or non-competitive.

Additionally, 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 and other early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

If we successfully obtain approval for any product candidate, we will face competition based on many different factors, including the safety and effectiveness of our products, the ease with which our products can be administered and the extent to which patients accept relatively new routes of administration, the timing and scope of regulatory approvals for these products, the availability and cost of manufacturing, marketing and sales capabilities, price, reimbursement coverage and patent position. Competing products could present superior treatment alternatives, including by being more effective, safer, more convenient, less expensive or marketed and sold more effectively than any of our products, if approved. Competitive products or technological approaches may make any products we develop, or our EDO platform, obsolete or noncompetitive before we recover the expense of developing and commercializing our product candidates. If we are unable to compete effectively, our opportunity to generate revenue from the sale of our products, if approved, could be adversely affected.

Sales and Marketing

We currently do not have a commercial infrastructure in any geography. As we progress our programs through development, we may build a commercial infrastructure in the U.S. and selected other territories to support the commercialization of each of our product candidates when we believe a regulatory approval in a particular territory is likely. We intend to conduct market research in connection with designing our commercialization strategy for each of our product candidates, which strategy may depend on the size and geographic dispersion of the target patient population and the characteristics of the prescribing audience for our products, if approved. For example, with respect to certain of our product candidates that target diseases with a limited patient population, a concentrated prescribing audience and a small number of key opinion leaders who influence the treatments prescribed for the relevant patient population, we may address each such market using our own targeted, specialty sales and marketing organization supported by internal sales personnel, an internal marketing group and distribution support. For other product candidates, we may establish a larger and more dispersed sales force, or seek strategic collaborations to support our commercialization efforts.

We intend to evaluate our commercialization strategy as we advance each product candidate through clinical development. In any core markets outside of the U.S. that we may identify, where appropriate, we may utilize strategic partners, distributors or contract sales forces to expand the commercial availability of our product candidates.

Material Contracts

License of Technology Agreement with Oxford University Innovation Limited and Medical Research Council as Part of United Kingdom Research and Innovation

On March 26, 2018, we, through our wholly-owned subsidiary PepGen Limited, entered into a license agreement, or the OUI/MRC License, with Oxford University Innovation Limited, or OUI, and MRC. We amended the OUI/MRC License on December 21, 2018, and subsequently amended and restated it on November 23, 2020.

Pursuant to the OUI/MRC License, we obtained from OUI and MRC an exclusive, royalty-bearing, sublicensable with consent (through one tier) license under certain patent rights, or the OUI/MRC Patents, and data, or the OUI/MRC Licensed Technology, and a nonexclusive, royalty-bearing, sublicensable (through one tier) license under certain know-how, or the OUI/MRC Know-How, for certain biological and chemical compounds, including compounds that comprise amino acids and/or nucleic acids relating to our EDO peptides, proprietary linkers and the resulting EDO conjugates. The Licensed Technology is incorporated in our product candidates PGN-EDO51, PGN-EDODM1, PGN-EDO53, PGN-EDO45 and PGN-EDO44, and will likely be utilized in future discovery programs. Under such licenses, we have the right to make, have made, import, use, sell, offer for sale, market, research, develop, trial, register, modify, enhance, improve, manufacture, have manufactured, hold, keep, formulate, optimize, have used, export, transfer, distribute, promote, have sold, dispose of, offer to dispose of or otherwise exploit in all fields of use on a worldwide basis any products or services that incorporate or otherwise utilize the OUI/MRC Licensed Technology or, in each such case, an OUI/MRC Licensed Product. We granted OUI, and those persons who at any time work or have worked on the OUI/MRC Licensed Technology and OUI/MRC Know-How, and MRC an irrevocable, perpetual, royalty-free, sublicensable license under the OUI/MRC Licensed Technology and OUI/MRC Know-How to use the OUI/MRC Licensed Technology and OUI/MRC Know-How for non-commercial clinical, research, teaching, publication, or other scholarly purposes, or Non-Commercial Purposes. MRC also retained the right to grant sublicenses under our rights in the OUI/MRC Licensed Technology and OUI/MRC Know-How for Non-Commercial Purposes to any person at MRC or any academic or not-for-profit institutions who have worked or collaborated on, or otherwise funded, the OUI/MRC Licensed Technology or OUI/MRC Know-How. Further, OUI, MRC and the Chancellor, Masters and Scholars of the University of Oxford retained the right to freely use, publish (subject to certain obligations) or grant licenses under the OUI/MRC Know-How.

The OUI/MRC License requires us to use commercially reasonable efforts to exploit the OUI/MRC Licensed Technology and to achieve certain development milestones in accordance with a development plan and commercialize the OUI/MRC Licensed Products.

In consideration for the rights conveyed by OUI and MRC under the OUI/MRC License, we were obligated to pay, and have paid, to OUI certain up-front fees in an aggregate amount of approximately £80,000 in connection with the execution of each of the original OUI/MRC License and the amended and restated OUI/MRC License. In addition, we are obligated to pay to OUI sub-single to low, single-digit percentage royalties, or the Royalty Rate, on net sales of any OUI/MRC Licensed Products in excess of a threshold amount between £20 million and £30 million that are commercialized by us. The royalty rate for a given OUI/MRC Licensed Product will decrease a certain percentage following expiration or revocation of the last valid claim of the OUI/MRC Patents covering such OUI/MRC Licensed Product and where there is a product sold by a third party that competes with such OUI/MRC Licensed Product on a country-by-country basis. If we receive any non-royalty payments and royalties in connection with sublicenses or other contracts

relating to the OUI/MRC Licensed Technology or OUI/MRC Know-How, we are obligated to pay to OUI, in each instance, a sublicense fee that is from mid-single digit to mid-teen percentage depending on the license year in which we execute the sublicense or contract. We are also required to pay certain milestone payments to OUI upon the achievement by us or our sublicensees of specified commercial milestone in an aggregate amount of £100,000 for certain OUI/MRC Licensed Products and specified patent procurement milestone in an aggregate amount of £10,000. In 2024, we paid OUI the patent procurement milestone of £10,000, adjusted per the retail price index under the terms of the OUI/MRC License.

Upon completion of our initial public offering, or IPO, in May 2022, we paid an exit fee of \$1.4 million to OUI during the second quarter of 2022.

Unless earlier terminated, the OUI/MRC License will terminate in its entirety upon the later of (a) the date on which all patents and patent applications licensed to us under the OUI/MRC License have been abandoned or allowed to lapse or expired or been rejected or revoked without a right of further appeal in a relevant country or territory or (b) March 26, 2038. The last-to-expire licensed patent under the OUI/MRC License is set to expire on February 11, 2042. We may terminate the OUI/MRC License in its entirety at any time for convenience upon providing OUI and MRC with written notice. Either party may terminate the OUI/MRC License in its entirety for the other party's uncured material breach after an opportunity for the other party to cure such material breach. OUI and MRC may terminate the OUI/MRC License for our (a) insolvency or if we challenge the validity of the licensed patents, (b) breach our obligation to develop and exploit the technology in accordance with the development plan and subsequent failure to take remedial action reasonably requested by OUI and/or MRC or (c) failure to pay the Exit Fee or Exit Buy Out Fee. If the OUI/MRC License is terminated by either party for any reason, the OUI/MRC Licenses will terminate and all rights thereunder will revert to OUI and MRC, respectively.

Intellectual Property

We seek to protect the intellectual property, or IP, and proprietary technology that we consider important to our business, including by pursuing patent applications that cover our product candidates and methods of using the same, as well as any other relevant inventions and improvements that are considered commercially important to the development of our business. We likewise seek to protect the IP to which we obtain rights through licenses and sublicenses (e.g., from universities and research institutions) and work collaboratively with our licensors to ensure (and if possible be the driver of) patent prosecution and protection. We also rely on trade secrets, know-how and continuing technological innovation to develop and maintain our proprietary and IP positions. Our commercial success depends, in part, on our ability to obtain, maintain, enforce and protect our intellectual property and other proprietary rights for the technology, inventions and improvements we consider important to our business, and to defend any patents we may own or in-license in the future, prevent others from infringing any patents we may own or in-license in the future, preserve the confidentiality of our trade secrets, and operate without infringing, misappropriating or otherwise violating the valid and enforceable patents and proprietary rights of third parties.

As with other biotechnology and pharmaceutical companies, our ability to maintain and solidify our proprietary and intellectual property position(s) for our product candidates and technologies will depend on our success in obtaining effective patent claims and enforcing those claims if granted. However, our pending patent applications, and any patent applications that we may in the future file or license from third parties, may not result in the issuance of patents and any issued patents we may obtain do not guarantee us the right to protect our technology in relation to the commercialization of our products. We also cannot predict the breadth of claims that may be allowed or enforced in any patents we may own or in-license in the future. Notwithstanding the scope of the patent protection available to us, a competitor could develop competitive products that are not covered by our intellectual property, and we may be unable to stop such competitor from commercializing such products.

Any issued patents that we may own or in-license in the future may be challenged, invalidated, circumvented or have the scope of their claims narrowed. Because patent applications can take many years to issue, there may be applications unknown to us, which applications may later result in issued patents that our existing or future products or technologies may be alleged to infringe. Additionally, we cannot be certain of the priority of inventions covered by pending third-party patent applications. If third parties prepare and file patent applications in the U.S. that also claim technology or therapeutics to which we have rights, we may have to participate in interference proceedings in the U.S. Patent and Trademark Office, or USPTO, to determine priority of invention, which is highly unpredictable and which could result in substantial costs, even if the eventual outcome is favorable to us. We are aware of certain patents in the U.S. and other jurisdictions owned by third parties that claim subject matter that relates to our product candidates and the EDO platform. In addition, because of the extensive time required for clinical development and regulatory review of a product candidate we may develop, it is possible that, before any of our product candidates can be commercialized, any patent covering a certain product may expire or remain in force for only a short period following commercialization, thereby limiting the protection such patent would afford the respective product and any competitive advantage such patent may provide.

The term of individual patents depends upon the date of filing of the patent application, the date of patent issuance and the legal term of patents in the countries in which they are obtained. In most countries, including the U.S., the patent term is 20 years from the earliest filing date of a non-provisional patent application. In the U.S., a patent's term may be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the USPTO in examining and granting a patent or may be shortened if a patent is terminally disclaimed over an earlier expiring patent.

The term of a patent claiming a new drug product may also be eligible for a limited patent term extension when FDA approval is granted, provided statutory and regulatory requirements are met. The restoration period granted on a patent covering a product is typically one-half the time between the effective date of a clinical investigation involving human beings is begun and the submission date of an application, plus the time between the submission date of an application and the ultimate approval date. The restoration period cannot be longer than five years and the total patent term, including the restoration period, must not exceed 14 years following

FDA approval. Only one patent applicable to an approved product is eligible for the extension, and only those claims covering the approved product, a method for using it, or a method for manufacturing it may be extended. Additionally, the application for the extension must be submitted prior to the expiration of the patent in question. A patent that covers multiple products for which approval is sought can only be extended in connection with one of the approvals. The USPTO reviews and approves the application for any patent term extension or restoration in consultation with the FDA. In the future, if our product candidates receive approval by the FDA, we expect to apply for patent term extensions on any issued patents covering those products, depending upon the length of the clinical studies for each product and other factors.

There can be no assurance that our pending patent applications will issue or that we will benefit from any patent term extension or favorable adjustments to the terms of any patents we may own or in-license in the future. In addition, the actual protection afforded by a patent varies on a product-by-product basis, from country-to-country, and depends upon many factors, including the type of patent, the scope of its coverage, the availability of regulatory-related extensions, the availability of legal remedies in a particular country and the validity and enforceability of the patent. Patent term may be inadequate to protect our competitive position on our products for an adequate amount of time.

In the future, we may need to engage in litigation to enforce patents issued or licensed to us, to protect our trade secrets or know-how or to defend against claims of infringement of the rights of others. Litigation could be costly and could divert our attention from other functions and responsibilities. Furthermore, even if our patents are found to be valid and infringed, a court may refuse to grant injunctive relief against the infringer and instead grant us monetary damages and/or ongoing royalties. Such monetary compensation may be insufficient to adequately offset the damage to our business caused by the infringer's competition in the market. Adverse determinations in litigation could subject us to significant liabilities to third parties, could require us to seek licenses from third parties and pay significant royalties to such third parties and could prevent us from manufacturing, selling or using our product or techniques, any of which could severely harm our business.

As of December 31, 2024, we owned three pending U.S. patent applications, one pending Patent Cooperation Treaty, or PCT, international application, two European patent applications, two Japanese patent applications, two Hong Kong patent applications, one Canadian patent application, and one Chinese patent application, and we exclusively licensed one issued European patent (validated in France, Germany, Italy, Spain, and Great Britain), one Saudi Arabian patent, and 76 pending patent applications under our OUI/MRC License. For more information regarding our OUI/MRC License, see the section titled "Business—Material Contracts—License of Technology Agreement with Oxford University Innovation Limited and Medical Research Council as Part of United Kingdom Research and Innovation."

The issued patent and patent applications that cover our product candidates and technology, as of December 31, 2024, include:

- With respect to PGN-EDO51, we owned applications pending in the U.S., Europe and Japan that cover methods of use and exclusively licensed 50 pending patent applications under the OUI/MRC License that cover compositions of matter and methods of use, including applications in Australia, Brazil, Canada, China, Europe, Hong Kong, Israel, India, Japan, South Korea, Mexico, New Zealand, the Russian Federation, Saudi Arabia, and the U.S. Any patents issuing from the patent applications would have expiration dates ranging from 2039 to 2042, without accounting for any available patent term adjustments or extensions.
- With respect to PGN-EDODM1, we owned applications pending in the U.S., Canada, China, Europe, Hong Kong, and Japan that cover methods of use and exclusively licensed one patent and 44 pending patent applications under the OUI/MRC License that cover compositions of matter and methods of use, including a patent in Saudi Arabia and applications in Australia, Brazil, Canada, China, Europe, Hong Kong, Israel, India, Japan, South Korea, Mexico, the Russian Federation, and the U.S. Any patents issuing from the patent applications would have expiration dates ranging from 2039 to 2042, without accounting for any available patent term adjustments or extensions.
- With respect to PGN-EDO53, PGN-EDO45 and PGN-EDO44, we owned one application pending in the U.S., and we exclusively licensed 30 pending patent applications under the OUI/MRC License that cover compositions of matter and methods of use, including applications in Australia, Brazil, Canada, China, Europe, Hong Kong, Israel, India, Japan, South Korea, Mexico, the Russian Federation, Saudi Arabia, and the U.S. Any patents issuing from these patent applications would expire in 2039 to 2045, without accounting for any available patent term adjustments or extensions.
- With respect to our EDO platform, we owned one pending PCT international patent application and exclusively licensed one issued European patent (validated in France, Germany, Italy, Spain, and Great Britain) and 42 pending patent applications under the OUI/MRC License that cover compositions of matter and methods of use, including applications in Australia, Brazil, Canada, China, Europe, Hong Kong, Israel, India, Japan, South Korea, Mexico, the Russian Federation, Saudi Arabia, and the U.S. The issued European patent is expected to expire in 2035, without accounting for any available patent term adjustments or extensions. The issued European patent was validated in France, Germany, Italy, Spain, and Great Britain, and it relates to certain compositions of matter and uses that may be utilized during future platform development activities. Any patents issuing from the patent applications would have expiration dates ranging from 2035 to 2043, without accounting for any available patent term adjustments or extensions.

Government Regulation

The FDA and comparable regulatory authorities in state and local jurisdictions and in other countries impose requirements upon companies involved in the clinical development, manufacture, marketing and distribution of drugs, such as those we are developing. These agencies and other federal, state and local entities regulate, among other things, the research and development, testing, manufacture, quality control, safety, effectiveness, labeling, storage, record keeping, approval, advertising and promotion, distribution, post-approval monitoring and reporting, sampling and export and import of drugs.

U.S. Government Regulation of Drug Products

In the U.S., the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and its implementing regulations. The process of obtaining regulatory approvals and the subsequent compliance with applicable federal, state, local and foreign statutes and regulations requires the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval, may subject an applicant to a variety of administrative or judicial sanctions, such as the FDA's refusal to approve pending New Drug Applications, or NDAs, withdrawal of an approval, imposition of a clinical hold, issuance of warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement or civil or criminal penalties.

The process required by the FDA before a drug may be marketed in the U.S. generally involves the following:

- Completion of preclinical laboratory tests, animal studies and formulation studies in compliance with the FDA's GLP regulations;
- Submission to the FDA of an IND, which must become effective before human clinical trials may begin;
- Approval by an independent institutional review board, or IRB, at each clinical site before each trial may be initiated;
- Performance of adequate and well-controlled human clinical trials in accordance with Good Clinical Practice, or GCP, requirements to establish the safety and efficacy of the proposed drug product for each proposed indication;
- Submission to the FDA of an NDA after completion of all pivotal trials, together with the payment of application user fees, as applicable;
- A determination by the FDA within 60 days of its receipt of an NDA to accept the marketing application for review;
- Satisfactory completion of an FDA advisory committee review, if applicable;
- Satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the product is produced to assess compliance with cGMP requirements and to assure that the facilities, methods and controls are adequate to preserve the product's identity, strength, quality and purity;
- Satisfactory completion of FDA audits of clinical trial sites to assure compliance with GCPs and the integrity of the clinical data; and
- FDA review and approval of the NDA.

Preclinical Studies

Before testing any drug product candidate, including our product candidates, in humans, the product candidate must undergo rigorous preclinical testing. Preclinical studies include laboratory evaluation of product chemistry, toxicity and formulation, as well as in vitro and animal studies to assess potential safety and efficacy. The conduct of preclinical studies is subject to federal regulations and requirements, including GLP regulations for safety/toxicology studies.

Prior to beginning the first clinical trial with a product candidate in the U.S., we must submit an IND to the FDA. An IND sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data and any available clinical data or literature and plans for clinical studies, among other things, to the FDA as part of an IND. An IND is a request for authorization from the FDA to administer an investigational product to humans and must become effective before human clinical trials may begin. Some preclinical testing, such as animal tests of reproductive adverse events and carcinogenicity, may continue even after the IND is submitted. An IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to one or more proposed clinical trials and places the clinical trial on a clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. As a result, submission of an IND may not result in the FDA allowing clinical trials to initiate.

Clinical Trials

Clinical trials involve the administration of the investigational new drug to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include the requirement that all research subjects provide their informed consent in writing for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other

things, the objectives of the trial, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. In addition, an IRB representing each institution participating in the clinical trial must review and approve the plan for any clinical trial before it is initiated at that institution. An IRB is charged with protecting the welfare and rights of trial participants and considers such items as whether the risks to individuals participating in the clinical trials are minimized and are reasonable in relation to anticipated benefits. The IRB also must review and approve the informed consent form that must be provided to each clinical trial subject or his or her legal representative and must monitor the clinical trial until completion.

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 DSMB, which provides authorization for whether or not a study may move forward at designated check points based on access to certain data from the study and may halt the clinical trial if it determines that there is an unacceptable safety risk for subjects or other grounds, such as no demonstration of efficacy.

Information about certain clinical trials must be submitted within specific timeframes to the National Institutes of Health, or NIH, for public dissemination on their www.clinicaltrials.gov website. Information related to the product, patient population, phase of investigation, study sites and investigators and other aspects of the clinical trial is made public as part of the registration of the clinical trial. Although sponsors are obligated to disclose the results of their clinical trials after completion, disclosure of the results can be delayed in some cases for some time. Failure to timely register a covered clinical study or to submit study results as provided for in the law can give rise to civil monetary penalties and also prevent the non-compliant party from receiving future grant funds from the federal government.

Human clinical trials are typically conducted in three sequential phases, which may overlap or be combined:

- Phase 1: The drug is initially introduced into healthy human subjects or patients with the target disease or condition and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an early indication of its effectiveness.
- Phase 2: The drug is administered to a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage.
- Phase 3: The drug is administered to an expanded patient population, generally at geographically dispersed clinical trial sites, in well-controlled clinical trials to generate enough data to statistically evaluate the efficacy and safety of the product for approval, to establish the overall risk-benefit profile of the product, and to provide adequate information for the labeling of the product. Generally, two adequate and well-controlled Phase 3 clinical trials are required by the FDA for approval of an NDA.

Post-approval trials, sometimes referred to as Phase 4 clinical trials, may be conducted after initial marketing approval. These trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication. In certain instances, the FDA may mandate the performance of Phase 4 clinical trials as a condition of approval on an NDA.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and more frequently if SAEs occur. Written IND safety reports must be submitted to the FDA and investigators for serious and unexpected suspected adverse events, findings from other studies or animal or in vitro testing that suggest a significant risk for human subjects and any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. The sponsor must submit an IND safety report within 15 calendar days after the sponsor determines that the information qualifies for reporting. The sponsor also must notify the FDA of any unexpected fatal or life-threatening suspected adverse reaction within seven calendar days after the sponsor's initial receipt of the information.

NDA Submission and FDA Review and Approval

Assuming successful completion of the required clinical testing, the results of the preclinical and clinical studies, together with detailed information relating to the product's chemistry, manufacture, controls and proposed labeling, among other things, are submitted to the FDA as part of an NDA requesting approval to market the product for one or more indications. Data may come from company-sponsored clinical trials intended to test the safety and effectiveness of a use of a product, or from a number of alternative sources, including studies initiated by investigators. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety and effectiveness of the investigational drug product for the proposed indication to the satisfaction of the FDA. In most cases, the submission of an NDA is subject to a substantial application user fee; a waiver of such fees may be obtained under certain limited circumstances.

The FDA conducts a preliminary review of all NDAs within the first 60 days after submission, before accepting them for filing, to determine whether they are sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA reviews an NDA to determine, among other things, whether the drug is safe and effective

and whether the facility in which it is manufactured, processed, packaged or held meets standards designed to assure the product's continued safety, quality and purity.

Under the Prescription Drug User Fee Act, or PDUFA, guidelines that are currently in effect, the FDA has a goal of ten months from the date of "filing" of a standard NDA, for a new molecular entity to review and act on the submission, and six months from the filing date of a new molecular entity NDA with priority review. Accordingly, this review process typically takes 12 months and eight months, respectively from the date the NDA is submitted to the FDA. The FDA does not always meet its PDUFA goal dates for standard or priority NDAs, and the review process is often extended by FDA requests for additional information or clarification. The FDA reviews an NDA to determine, among other things, whether the drug is safe and effective and whether the facility in which it is manufactured, processed, packaged or held meets standards designed to assure the product's continued safety, quality and purity.

In addition, under the Pediatric Research Equity Act of 2003, or PREA, as amended, certain NDAs or supplements to an NDA must contain data that are adequate to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements. A sponsor who is planning to submit a marketing application for a drug that includes a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration must submit an initial Pediatric Study Plan, or PSP, within 60 days of an end-of-Phase 2 meeting or, if there is no such meeting, as early as practicable before initiation of the Phase 3 or Phase 2/3 study. The initial PSP must include an outline of the pediatric study or studies that the sponsor plans to conduct, including study objectives and design, age groups, relevant endpoints and statistical approach, or a justification for not including such detailed information, and any request for a deferral of pediatric assessments or a full or partial waiver of the requirement to provide data from pediatric studies along with supporting information. The FDA and the sponsor must reach an agreement on the PSP. A sponsor can submit amendments to an agreed-upon initial PSP at any time if changes to the pediatric plan need to be considered based on data collected from preclinical studies, early phase clinical trials and/or other clinical development programs.

The FDA may refer an application for a novel drug or a drug that presents difficult questions of safety or efficacy to an advisory committee. An advisory committee is a panel of independent experts, including clinicians and other scientific experts, which reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

The FDA also may require the submission of a Risk Evaluation and Mitigation Strategy, or REMS, if it determines that a REMS is necessary to ensure that the benefits of the drug outweigh its risks and to assure the safe use of the drug. A REMS may include one or more elements, including medication guides, physician communication plans, patient package insert and/or elements to assure safe use, such as restricted distribution methods, patient registries or other risk minimization tools. The FDA determines the requirement for a REMS, as well as the specific REMS provisions, on a case-by-case basis. If the FDA concludes a REMS is needed, the sponsor of the NDA must submit a proposed REMS. The FDA will not approve the NDA without a REMS, if required.

Before approving an NDA, the FDA typically will inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA may inspect one or more clinical trial sites to assure compliance with GCP requirements.

After evaluating the NDA and all related information, including the advisory committee recommendation, if any, and inspection reports regarding the manufacturing facilities and clinical trial sites, the FDA may issue an approval letter, or, in some cases, a Complete Response Letter. A Complete Response Letter indicates that the review cycle of the application is complete, and the application will not be approved in its present form. A Complete Response Letter generally outlines the deficiencies in the submission and contains a statement of specific conditions that must be met in order to secure final approval of the NDA; it may require additional clinical or preclinical testing in order for FDA to reconsider the application. If a Complete Response Letter is issued, the applicant may either resubmit the NDA, addressing all of the deficiencies identified in the letter, or withdraw the application. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. If and when those conditions have been met to the FDA's satisfaction, the FDA will typically issue an approval letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications.

Even if the FDA approves a product, it may limit the approved indications for use of the product, require that contraindications, warnings or precautions be included in the product labeling, require that post-approval studies, including Phase 4 clinical trials, be conducted to further assess a drug's safety after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution and use restrictions or other risk management mechanisms under a REMS, which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-marketing studies or surveillance programs. After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes, and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Orphan Drug Designation and Exclusivity

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug product intended to treat a rare disease or condition, which is generally a disease or condition that affects either (i) fewer than 200,000 individuals in the U.S., or (ii) more than 200,000 individuals in the U.S. and for which there is no reasonable expectation that the cost of developing and making the product

available in the U.S. for this type of disease or condition will be recovered from sales of the product. A company must request orphan drug designation before submitting an NDA. If the request is granted, the FDA will disclose the identity of the therapeutic agent and its potential use. Orphan drug designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If a product with orphan status receives the first FDA approval for the disease or condition for which it has such designation or for a select indication or use within the rare disease or condition for which it was designated, the product is entitled to orphan product exclusivity. Orphan product exclusivity means that the FDA may not approve any other applications to market the same product for the same indication for seven years, except in certain limited circumstances. Orphan exclusivity will not bar approval of another product under certain circumstances, including if a subsequent product with the same active ingredient for the same indication is shown to be clinically superior to the approved product on the basis of greater efficacy or safety, or providing a major contribution to patient care, or if the company with orphan drug exclusivity is not able to meet market demand. Further, the FDA may approve more than one product for the same orphan indication or disease as long as the products contain different active ingredients. Moreover, competitors may receive approval of different products for the indication for which the orphan product has exclusivity or obtain approval for the same product but for a different indication for which the orphan drug has exclusivity. Other benefits of orphan drug designation include tax credits for certain research and waiver from the NDA application fee.

A designated orphan drug may not receive orphan drug exclusivity if it is approved for a use that is broader than the indication for which it received orphan designation. In addition, orphan drug exclusive marketing rights in the U.S. may be lost if the FDA later determines that the request for designation was materially defective or, as noted above, if a 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.

Expedited Development and Review Programs

The FDA maintains several programs intended to facilitate and expedite development and review of new drugs to address unmet medical needs in the treatment of serious or life-threatening diseases or conditions. These programs include Fast Track designation, Breakthrough Therapy designation, Priority Review and Accelerated Approval, and the purpose of these programs is to either expedite the development or review of important new drugs to get them to patients earlier than under standard FDA development and review procedures.

The FDA has a Fast Track designation program that is intended to expedite or facilitate the process for reviewing new drugs that meet certain criteria. Specifically, new drugs are eligible for Fast Track designation if they are intended to treat a serious or life threatening condition and preclinical or clinical data demonstrate the potential to address unmet medical needs for the condition. Fast Track designation applies to both the product and the specific indication for which it is being studied. The sponsor can request that the FDA grant the product Fast Track designation any time before receiving NDA approval, but ideally no later than the pre-NDA meeting. Fast Track designation provides increased opportunities for sponsor interactions with the FDA review team to expedite development and review of the product. The FDA may also review sections of the NDA for a Fast Track designated-product 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. Fast Track designation may be lost if the designation is no longer supported by data emerging in the clinical trial process.

Additionally, a drug may be eligible for designation as a breakthrough therapy if the product is intended, alone or in combination with one or more other drugs or biologics, to treat a serious or life-threatening condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over currently approved therapies on one or more clinically significant endpoints. The benefits of Breakthrough Therapy designation include the same benefits as Fast Track designation, plus intensive guidance from the FDA to ensure an efficient drug development program. Breakthrough therapy designation comes with all of the benefits of Fast Track designation, which means that the sponsor may file sections of the NDA for review on a rolling basis if certain conditions are satisfied, including an agreement with the FDA on the proposed schedule for submission of portions of the application and the payment of applicable user fees before the FDA may initiate a review. A product may also be eligible for priority review if it treats a serious or life-threatening condition and, if approved, would provide a significant improvement in safety and effectiveness compared to available therapies. The FDA determines at the time that the marketing application is submitted, on a case-by-case basis, whether the proposed drug represents a significant improvement in treatment, prevention or diagnosis of disease when compared with other available therapies. A priority review designation is intended to direct overall attention and resources to the evaluation of such applications and to shorten the FDA's goal for taking action on a marketing application from ten months to six months for an NDA for a new molecular entity from the date of filing. If criteria are not met for priority review, the application for a new molecular entity is subject to the standard FDA review period of ten months after FDA accepts the application for filing. Priority review designation does not change the scientific/medical standard for approval or the quality of evidence necessary to support approval.

A product may also be eligible for accelerated approval if it treats a serious or life-threatening disease or condition, generally provides a meaningful advantage over available therapies and demonstrates an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, or IMM, that is reasonably likely to predict an effect on IMM or other clinical benefit, taking into account the severity, rarity or prevalence of the condition and the availability or lack of alternative treatments. As a condition of accelerated approval, the FDA generally requires that a sponsor perform adequate and well-controlled post-marketing clinical trials to verify and describe the product's clinical benefit. These confirmatory trials must be completed with due diligence, and, under the Food and Drug Omnibus Reform Act of 2022, or

FDORA, the FDA is now permitted to require, as appropriate, that such trials be underway prior to approval or within a specific time period after the date of approval for a product granted accelerated approval. Under FDORA, the FDA has increased authority for expedited procedures to withdraw the product from the market (and withdraw its approval). In addition, for products being considered for accelerated approval, the FDA generally requires, unless otherwise informed by the agency, pre-approval of promotional materials, which could adversely impact the timing of the commercial launch of the product.

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. Fast Track designation, Breakthrough Therapy designation, priority review and accelerated approval do not change the standards for approval and may not ultimately expedite the development or approval process.

U.S. Non-Patent Exclusivity

Market exclusivity provisions under the FDCA can delay the submission or the approval of certain follow-on applications. The FDCA provides a five-year period of data exclusivity within the U.S. to the first applicant to gain approval of an NDA for a new chemical entity, or NCE. A drug is a NCE if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not accept for review an Abbreviated New Drug Application, or ANDA, for a generic version of the drug or a 505(b)(2) NDA for another version of such drug where the applicant does not own or have a legal right of reference to all the data required for approval. However, such a follow-on application may be submitted after four years if it contains a certification of patent invalidity or non-infringement to one of the patents listed with the FDA by the innovator NDA holder.

The FDCA also provides three years of market exclusivity for an NDA, 505(b)(2) NDA or supplement to an existing NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example, new indications, dosages or strengths of an existing drug. This three-year exclusivity period covers only the conditions of use associated with the new clinical investigations and does not prohibit the FDA from approving follow-on applications that do not reference the protected clinical data. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

Pediatric exclusivity is another type of regulatory market exclusivity in the U.S. Pediatric exclusivity, if granted, adds six months to existing regulatory exclusivity periods for all formulations, dosage forms, and indications of the active moiety and listed patent terms. This six-month exclusivity may be granted based on the voluntary completion of a pediatric trial in accordance with an FDA-issued "Written Request" for such a trial, provided that at the time pediatric exclusivity is granted there is not less than nine months of term remaining. The issuance of a Written Request does not require the sponsor to undertake the described clinical trials.

Post-approval Requirements

Drugs manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with 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 are continuing, annual user fee requirements for any marketed products.

The FDA may impose a number of post-approval requirements as a condition of approval of an NDA. For example, the FDA may require post-marketing testing, including Phase 4 clinical trials, and surveillance to further assess and monitor the product's safety and effectiveness after commercialization.

FDA regulations require that products be manufactured in specific facilities and in accordance with cGMP regulations which require, among other things, quality control and quality assurance, the maintenance of records and documentation and the obligation to investigate and correct any deviations from cGMP. In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved drugs and those supplying products, ingredients, and components of them are required to register their establishments with the FDA and state agencies, and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with cGMP requirements. Manufacturers and other parties involved in the drug supply chain for prescription drug products must also comply with product tracking and tracing requirements and for notifying FDA of counterfeit, diverted, stolen and intentionally adulterated products or products that are otherwise unfit for distribution in the U.S. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP requirements and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance.

Once an approval of a drug is granted, the FDA may withdraw the 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 mandatory revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Any of these limitations on approval or marketing could restrict the commercial promotion, distribution, prescription or dispensing of products. 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 clinical holds on post-approval clinical trials;
- Refusal of the FDA to approve pending NDAs or supplements to approved NDAs, or suspension or withdrawal of product 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;
- Issuance of safety alerts, Dear Healthcare Provider letters, press releases and other communications containing warnings or other safety information about the product; and
- Injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Drugs may be promoted by a manufacturer and any third parties acting on behalf of a manufacturer only for the approved indications and in a manner consistent with the approved label for the product. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability. 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, in their independent professional medical judgment, 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. 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. The federal government has levied large civil and criminal fines against companies for alleged improper promotion of off-label use and has enjoined companies from engaging in off-label promotion. The FDA and other regulatory agencies have also required that companies enter into consent decrees and/or imposed permanent injunctions under which specified promotional conduct is changed or curtailed. However, companies may share truthful and not misleading information that is otherwise consistent with a product's FDA-approved labeling.

From time to time, legislation is drafted, introduced, passed in Congress and signed into law that could significantly change the statutory provisions governing the approval, manufacturing, and marketing of products regulated by the FDA. In addition to new legislation, FDA regulations, guidances, and policies are often revised or reinterpreted by the agency in ways that may significantly affect the manner in which pharmaceutical products are regulated and marketed

Healthcare Regulation

Coverage and Reimbursement

Sales of any product depend, in part, on the extent to which such product will be covered by third-party payors, such as federal, state, and foreign government healthcare programs, commercial insurance and managed healthcare organizations, and the level of reimbursement for such product by third-party payors. Decisions regarding the extent of coverage and amount of reimbursement to be provided are made on a plan-by-plan basis. These third-party payors are increasingly reducing coverage and reimbursement for medical products, drugs and services. 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. Additionally, separate reimbursement for the product itself or the treatment or procedure in which the product is used may not be available, which may impact physician utilization.

The U.S. government, state legislatures and foreign governments have also continued implementing cost-containment programs, including price controls, restrictions on coverage and reimbursement and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit sales of any product. Decreases in third-party reimbursement for any product or a decision by a third-party payor not to cover a product could reduce physician usage and patient demand for the product and also have a material adverse effect on sales.

Other Healthcare Laws

Pharmaceutical companies are subject to additional healthcare regulation and enforcement by the federal government and by authorities in the states and foreign jurisdictions in which they conduct their business that may constrain the financial arrangements and relationships through which we research, as well as sell, market and distribute any products for which we obtain marketing authorization. Such laws include, without limitation, state and federal anti-kickback, fraud and abuse, false claims, and transparency laws and regulations related to drug pricing and payments and other transfers of value made to physicians and other healthcare providers. If our operations are found to be in violation of any of such laws or any other governmental regulations that apply, we may be subject to penalties, including, without limitation, administrative, civil and criminal penalties, damages, fines, disgorgement, the

curtailment or restructuring of operations, integrity oversight and reporting obligations, exclusion from participation in federal and state healthcare programs and responsible individuals may be subject to imprisonment.

Healthcare Reform and Legislative Updates

In the U.S., in 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, each as amended, collectively known as the ACA, was enacted, which substantially changed the way healthcare is financed by both governmental and private insurers, and significantly affected the pharmaceutical industry. The ACA contained a number of provisions, including those governing enrollment in federal healthcare programs, reimbursement adjustments and changes to fraud and abuse laws. For example, the ACA:

- increased the minimum level of Medicaid rebates payable by manufacturers of brand name drugs;
- required collection of rebates for drugs paid by Medicaid managed care organizations;
- required manufacturers to participate in a coverage gap discount program, under which they must agree to offer 70 percent point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D; and
- imposed a non-deductible annual fee on pharmaceutical manufacturers or importers who sell "branded prescription drugs" to specified federal government programs.

Other legislative changes have been proposed and adopted since the ACA was enacted, including aggregate reductions of Medicare payments to providers of 2% per fiscal year through 2031, unless additional Congressional action is taken. The American Rescue Plan Act of 2021 eliminated the statutory Medicaid drug rebate cap, previously set at 100% of a drug's average manufacturer price, for single source and innovator multiple source drugs, effective January 1, 2024. Due to the Statutory Pay-As-You-Go Act of 2010, estimated budget deficit increases resulting from the American Rescue Plan Act of 2021, and subsequent legislation, Medicare payments to providers will be further reduced starting in 2025 absent further legislation. These laws and regulations may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used.

Further, the Inflation Reduction Act of 2022 (IRA) included several provisions that may impact our business to varying degrees, including provisions that reduce the out-of-pocket spending cap for Medicare Part D beneficiaries from \$7,050 to \$2,000 starting in 2025, thereby effectively eliminating the coverage gap; impose new manufacturer financial liability on certain drugs under Medicare Part D, allow the U.S. government to negotiate Medicare Part B and Part D price caps for certain high-cost drugs and biologics without generic or biosimilar competition; require companies to pay rebates to Medicare for certain drug prices that increase faster than inflation; and delay until January 1, 2032 the implementation of the HHS rebate rule that would have limited the fees that pharmacy benefit managers can charge. Further, under the IRA, orphan drugs are exempted from the Medicare drug price negotiation program, but only if they have one orphan designation and for which the only approved indication is for that disease or condition. If a product receives multiple orphan designations or has multiple approved indications, it may not qualify for the orphan drug exemption. The implementation of the IRA is currently subject to ongoing litigation challenging the constitutionality of the IRA's Medicare drug price negotiation program. The implementation of the IRA is currently subject to ongoing litigation challenging the constitutionality of the IRA's Medicare drug price negotiation program. The effects of the IRA on our business and the healthcare industry in general is not yet known.

Moreover, there has recently been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries, proposed and enacted legislation and executive orders designed to, among other things, bring more transparency to product pricing, reduce the cost of prescription drugs, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products. Individual states in the U.S. have also become increasingly active in implementing regulations designed to control pharmaceutical product 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.

We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could impact the amounts that federal and state governments and other third-party payors will pay for healthcare products and services.

Data Privacy and Security

Numerous state, federal and foreign laws, regulations and standards govern the collection, use, access to, confidentiality and security of health-related and other personal information, and could apply now or in the future to our operations or the operations of our partners. In the U.S., numerous federal and state laws and regulations, including data breach notification laws, health information privacy and security laws and consumer protection laws and regulations govern the collection, use, disclosure, and protection of health-related and other personal information. In addition, certain foreign laws govern the privacy and security of personal data, including health-related data. For example, European Union General Data Protection Regulation (EU) 2016/679, or the GDPR imposes strict requirements for processing the personal data of individuals within the European Economic Area, or EEA, including requirements relating to processing health-related and other sensitive data, establishing a legal basis for processing such as obtaining

consent of the individuals to whom the personal data relates, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches, imposing limitations on retention of personal data; maintaining a record of data processing, complying with the principal of accountability and the obligation to demonstrate compliance through policies, procedures, training and audit and taking certain measures when engaging third-party processors. The GDPR also imposes strict rules on the transfer of personal data to countries outside the EEA to countries that the European Union, or EU does not consider to have in place adequate data protection legislation, including the U.S. 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 non-compliant company, whichever is greater. Further, from January 1, 2021, companies have had to comply with the GDPR and also the UK GDPR, which, together with the amended UK Data Protection Act 2018, retains the GDPR in the U.K., or UK national law. 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.

Regulation and Procedures Governing Approval of Medicinal Products Outside the United States

In order to market any product outside of the United States, a company must also comply with numerous and varying regulatory requirements of other countries and jurisdictions regarding quality, safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of products. Whether or not it obtains FDA approval for a product, an applicant will need to obtain the necessary approvals by the comparable foreign regulatory authorities before it can commence clinical trials or marketing of the product in those countries or jurisdictions. For example, the process governing approval of medicinal products in the EU generally follows the same lines as in the United States. It entails satisfactory completion of preclinical studies and adequate and well-controlled clinical trials to establish the safety and efficacy of the product for each proposed indication. It also requires the submission to the relevant competent authorities of a marketing authorization application, and granting of a marketing authorization by these authorities before the product can be marketed and sold in the EU.

European Union Drug Development and Approval

Clinical Trial Approval

In April 2014, the EU adopted the Clinical Trials Regulation (EU) No 536/2014, or CTR, which repealed and replaced the previous Clinical Trials Directive (2001/20/EC) on January 31, 2022. The transitory provisions of the CTR provide that all ongoing clinical trials must have transitioned to the CTR by January 31, 2025. The CTR overhauls the previous system of approvals for clinical trials in the EU. Specifically, the CTR, which is directly applicable in all EU Member States (meaning no national implementing legislation in each Member State is required), aims at simplifying and streamlining the approval of clinical trials in the EU, simplifying adverse-event reporting procedures, improving the supervision of clinical trials and increasing their transparency. The main characteristics of the CTR include: a streamlined application procedure via a single-entry point through the Clinical Trials Information System, or CTIS; a single set of documents to be prepared and submitted for the application as well as simplified reporting procedures for clinical trial sponsors; and a harmonized procedure for the assessment of applications for clinical trials. The role of the relevant ethics committees in the assessment procedure continues to be governed by the national law of the applicable Member State, however overall related timelines are defined by the CTR.

Marketing Authorization

To obtain a marketing authorization for a product in the EU, an applicant must submit a marketing authorization application, either under a centralized procedure administered by the European Medicines Agency, or EMA, or one of the procedures administered by competent authorities in the EU Member States (decentralized procedure, national procedure, or mutual recognition procedure). A marketing authorization may be granted only to an applicant established in the EU or the additional Member States of the European Economic Area (Norway, Iceland and Liechtenstein), or EEA.

The centralized procedure provides for the grant of a single marketing authorization by the European Commission that is valid for all EU Member States, as well as the additional Member States of the EEA. Pursuant to Regulation (EC) No. 726/2004, the centralized procedure is compulsory for specific products, including for medicines produced by certain biotechnological processes, products designated as orphan medicinal products, advanced therapy medicinal products (gene-therapy, somatic cell-therapy or tissue-engineered medicines) and products with a new active substance indicated for the treatment of cancer, HIV, AIDS, neurodegenerative disorders, diabetes, auto-immune and other immune dysfunctions or 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 Committee for Medicinal Products for Human Use, or CHMP, established at the EMA is responsible for conducting an initial assessment of a product. The maximum timeframe for the evaluation of a marketing authorization application is 210 days, excluding clock stops when additional information or written or oral explanation is to be provided by the applicant in response to questions of the CHMP. Clock stops may extend the timeframe of evaluation of an application considerably beyond 210 days. Where the CHMP gives a positive opinion, the EMA provides the opinion together with supporting documentation to the European Commission, who makes the final decision to grant a marketing authorization, which is issued within 67 days of receipt of the EMA's recommendation. Accelerated evaluation may be granted by the CHMP in exceptional cases, when a medicinal product is of major interest from the viewpoint of public health and, in particular, therapeutic innovation. If the CHMP accepts such a

request, the time limit of 210 days will be reduced to 150 days, but it is possible that the CHMP may revert to the standard time limit for the centralized procedure if it determines that it is no longer appropriate to conduct an accelerated assessment.

National marketing authorizations, which are issued by the competent authorities of the Member States of the EU and only cover their respective territory, are available for products not falling within the mandatory scope of the centralized procedure. Where a product has already been authorized for marketing in a Member State of the EU, this national authorization can be recognized in other Member States through the mutual recognition procedure. If the product has not received a national authorization in any Member State at the time of application, it can be approved simultaneously in various Member States through the decentralized procedure.

Data and Market Exclusivity in the European Union

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

Orphan Designation and Exclusivity

Regulation (EC) No 141/2000 and Regulation (EC) No. 847/2000 provide that a product can be designated as an orphan medicinal product by the European Commission if its sponsor can establish that: (1) the product is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition, (2) either (i) such condition affects no more than five in ten thousand persons in the EU when the application is made, or (ii) without the benefits derived from orphan status, it is unlikely that the marketing of the product in the EU would generate sufficient return to justify the necessary investment in its development; (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 would be of significant benefit to those affected by that condition.

An orphan designation provides a number of benefits, including fee reductions, regulatory assistance and the possibility to apply for a centralized EU marketing authorization. Marketing authorization for an orphan medicinal product leads to a ten-year period of market exclusivity being granted following marketing approval of the orphan product. During this market exclusivity period, the EMA, the European Commission or the competent authorities of the EU Member States may only grant marketing authorization to a "similar medicinal product" for the same therapeutic indication if: (i) a second applicant can establish that its product, although similar to the authorized product, is safer, more effective or otherwise clinically superior; (ii) the marketing authorization holder for the authorized product consents to a second orphan medicinal product application; or (iii) the marketing authorization holder for the authorized product cannot supply enough orphan medicinal product. A "similar medicinal product" is defined as a medicinal product containing a similar active substance or substances as contained in an authorized orphan medicinal product, and which is intended for the same therapeutic indication. The market exclusivity period for the authorized therapeutic indication 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 because, for example, the product is sufficiently profitable not to justify market exclusivity. Orphan designation must be requested before submitting an application for marketing approval. Orphan designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

The aforementioned EU rules are generally applicable in the EEA.

Reform of the Regulatory Framework in the European Union

The European Commission introduced legislative proposals in April 2023 that, if implemented, will replace the current regulatory framework in the EU for all medicines (including those for rare diseases and for children). The European Commission has provided the legislative proposals to the European Parliament and the European Council for their review and approval, and, in April

2024, the European Parliament proposed amendments to the legislative proposals. Once the European Commission's legislative proposals are approved (with or without amendment), they will be adopted into EU law.

Brexit and the Regulatory Framework in the United Kingdom

The U.K. formally left the EU on January 31, 2020, and the EU and the U.K. have concluded a trade and cooperation agreement, or TCA, which was provisionally applicable since January 1, 2021 and has been formally applicable since May 1, 2021. The TCA includes specific provisions concerning pharmaceuticals, which include the mutual recognition of cGMP, inspections of manufacturing facilities for medicinal products and cGMP documents issued, but does not provide for wholesale mutual recognition of United Kingdom and EU pharmaceutical regulations. At present, EU laws which have been transposed into U.K. law through secondary legislation continue to be applicable as "retained EU law". However, legislation such as the EU Clinical Trials Regulation or other new EU legislation in relation to orphan medicinal products are not applicable. The U.K. government has passed the Medicines and Medical Devices Act 2021, which introduced delegated powers in favor of the Secretary of State (or for Northern Ireland, the Department of Health in Northern Ireland) 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.

As a result of the Northern Ireland protocol, following Brexit, the EMA remained responsible for approving novel medicines for supply in Northern Ireland under the EU centralized procedure, and a separate authorization was required to supply the same medicine in Great Britain (England, Wales and Scotland). However, on February 27, 2023, the U.K. government and the European Commission announced a political agreement in principle to replace the Northern Ireland Protocol with a new set of arrangements, known as the "Windsor Framework". This new framework fundamentally changes the existing system under the Northern Ireland Protocol, including with respect to the regulation of medicinal products in the U.K.. In particular, the MHRA is now responsible for approving all medicinal products destined for the U.K. market (i.e., Great Britain and Northern Ireland), and the EMA will no longer have any role in approving medicinal products destined for Northern Ireland under the EU centralized procedure. A single U.K.-wide marketing authorization will be granted by the MHRA for all novel medicinal products to be sold in the U.K., enabling products to be sold in a single pack and under a single authorization throughout the U.K. In addition, the new arrangements require all medicines placed on the U.K. market to be labelled "UK only", indicating they are not for sale in the EU. The medicinal product aspects of the Windsor Framework have applied since January 1, 2025.

The MHRA has also 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. On January 1, 2024, a new international recognition framework was put in place, under which the MHRA may have regard to decisions on the approval of marketing authorizations made by the European Medicines Agency and certain other regulators (including the FDA) when determining an application for a U.K. authorization. The MHRA also has the power to have regard to marketing authorizations approved in EU Member States (or Iceland, Liechtenstein, Norway) through decentralized or mutual recognition procedures when determining an application for a U.K. authorization.

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

Pricing Decisions for Approved Products

In the EU, pricing and reimbursement schemes vary widely from country to country. Some countries provide that products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost-effectiveness of a particular product candidate to currently available therapies or so-called health technology assessments, in order to obtain reimbursement or pricing approval. For example, EU Member States have the option to restrict the range of products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. EU Member States may approve a specific price for a product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the product on the market. Other EU Member States allow companies to fix their own prices for products, but monitor and control prescription volumes and issue guidance to physicians to limit prescriptions. Recently, many countries in the EU have increased the amount of discounts required on pharmaceuticals and these efforts could continue as countries attempt to manage health care expenditures, especially in light of the severe fiscal and debt crises experienced by many countries in the EU. The downward pressure on health care costs in general, particularly prescription products, has become intense.

As a result, increasingly high barriers are being erected to the entry of new products. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various EU Member States, and parallel trade, i.e., arbitrage between low-priced and high-priced

EU Member States, can further reduce prices. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any products, if approved in those countries.

Rest of the World Regulation

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

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

Employees and Human Capital Resources

As of December 31, 2024, we had 81 full-time employees, of whom 27 have Ph.D. degrees, and several part-time employees employed on a co-op or internship basis. Within our workforce, 65 employees are engaged in research and development and 16 are engaged in finance, legal, business development, and general management and administration. None of our employees are represented by labor unions or covered by collective bargaining agreements. We consider our relationship with our employees to be good.

Our human capital resources objectives include, as applicable, identifying, recruiting, retaining, incentivizing and integrating our existing and new employees, advisors and consultants. The principal purposes of our equity incentive plans are to attract, retain and reward personnel through the granting of equity-based compensation awards in order to increase stockholder value and the success of our company by motivating such individuals to perform to the best of their abilities and achieve our objectives.

Facilities

In 2024, we primarily operated out of 31,668 square feet of office and laboratory space at 321 Harrison Street, Boston, Massachusetts 02118. The lease was signed on December 1, 2021 and the lease term commenced on December 29, 2022. The term of the lease is 110 months from the commencement date, expiring in May 2032, with an option to extend the lease for one successive five-year term.

We believe that our facilities are adequate for our current needs and for the foreseeable future. To meet the future needs of our business, we may lease additional or alternate space. We believe that suitable additional or substitute space at commercially reasonable terms will be available as needed to accommodate any future expansion of our operations.

Our Culture and Team

Our mission is to deliver transformative therapeutics to those in need, and we believe our innovative EDO technology is well-positioned to effect this change for patients, families and the broader healthcare community. As a company, we value:

- **Research:** We are a data-driven scientific company at heart, and we approach our work with an evidence-based mindset;
- **Innovation:** We are always exploring new ways to learn, build and improve across all facets of our company;
- **Integrity:** We act ethically and honestly in both our scientific and business conduct; and
- **Responsibility:** As a therapeutic company, we appreciate the impact our work has on patients and their families.

In support of our mission, we have assembled a leadership team with deep experience in research and development, clinical translation, regulatory affairs, corporate development and compliance. Our Chief Executive Officer, James McArthur, Ph.D., brings over 25 years of industry experience to the company, including senior leadership and Board roles at Imara Inc., Cydan LLC and Nightstar Therapeutics plc, with a specific focus on rare disease therapeutics. Dr. McArthur is ably supported by Noel Donnelly, M.B.A., our Chief Financial Officer, who has over 25 years of experience in financial planning and analysis, business analytics and portfolio management and has held roles at EIP Pharma Inc., Takeda Pharmaceuticals, Inc., and Shire HGT; Paul Streck, M.D., M.B.A., our Head of Research and Development, who has over 20 years of experience in drug development, regulatory, and medical affairs leadership, and has held roles at Albireo Pharma, Inc., Arena Pharmaceuticals, Alder Biopharmaceuticals Inc., and Inmed Incorporated, as well as progressive roles at GSK, Shire HGT, and Amgen Inc., and 10 years in academic medical practice; Mary Beth DeLena, our General Counsel and Secretary, who has over 20 years of experience advising life sciences companies in a broad range of strategic, transactional, and corporate matters, spanning early research and development to commercial launch and execution, and has held roles at Alnylam, Praecis Pharmaceuticals, Inc. and Skadden, Arps, Slate, Meagher & Flom LLP; and David Borah, CFA, our Senior Vice President of Investor Relations and Corporate Communications, who spent over 20 years on the buy-side, holding

numerous equity research positions of increasing responsibility at GW&K Investment Management, Newton Investment Management (formerly The Boston Company Asset Management), and Century Capital Management, and most recently held roles at Mural Oncology plc and Bicycle Therapeutics plc. We have also established a strong scientific advisory board, with members who bring a wealth of expertise from both the indication and therapeutic modality perspectives in their roles as academics, clinicians and drug developers.

We were founded in 2018 with technology spun out from the University of Oxford and MRC to further develop and commercialize this novel peptide delivery approach. This technology was created and refined over a decade by Michael Gait, Ph.D. and Professor Matthew Wood, M.D., Ph.D. We have exclusively licensed the patents, patent applications and know-how associated with this technology.

Item 1A. Risk Factors.

Investing in our common stock involves a high degree of risk. You should carefully read and consider all of the risks described below, as well as the other information in this 10-K, including our financial statements and the related notes and the section titled “Management’s Discussion and Analysis of Financial Condition and Results of Operations,” and in other documents we file with the SEC when evaluating our business. The occurrence of any of the events or developments described below could harm our business, financial condition, results of operations and growth prospects. Unless otherwise indicated, references to our business being harmed in these risk factors will include harm to our business, reputation, financial condition, results of operations and future prospects. In such an event, the market price of our common stock could decline, and you may lose all or part of your investment. The risks described below are not intended to be exhaustive and are not the only risks that we face. Additional risks and uncertainties not presently known to us or that we currently deem immaterial also may impair our business operations and the market price of our common stock.

Risks Related to Our Financial Position and Need for Additional Capital

We have incurred significant losses since our inception, have no products approved for sale and we expect to incur losses for the foreseeable future.

Since inception, we have incurred significant operating losses. Our net losses were \$90.0 million and \$78.6 million for the years ended December 31, 2024 and December 31, 2023, respectively. As of December 31, 2024, we had an accumulated deficit of \$271.5 million. To date, we have financed our operations primarily with the proceeds raised from the sale of our convertible preferred stock in private placements and common stock in our IPO and our equity offerings in early 2024, described below. We have devoted substantially all of our financial resources and efforts to research and development activities, business planning, establishing and maintaining our intellectual property portfolio, acquiring and developing product and technology rights, hiring personnel, leasing premises and associated capital expenditures, raising capital, and providing general and administrative support for these operations. We are still in the early stages of development of our programs and have only advanced two product candidates into clinical development. We expect to continue to incur significant expenses and operating losses for the foreseeable future. Our operating expenses and net losses may fluctuate significantly from quarter to quarter and year to year. We anticipate that our expenses will increase substantially if and as we:

- continue to advance our programs in DMD and DM1 through clinical development and work to resolve the U.S. clinical hold on the initiation in the U.S. of the CONNECT1 Phase 2 study of PGN-EDO51 in DMD;
- advance any additional product candidates we identify through our research programs into IND- or CTA-enabling studies and clinical trials following regulatory clearance to commence clinical research;
- continue to develop and expand the capabilities of our proprietary EDO platform;
- establish manufacturing sources for our product candidates and secure supply chain capacity to provide sufficient quantities for preclinical and clinical development and commercial supply;
- seek marketing approvals for any product candidates that successfully complete pivotal clinical trials;
- obtain, expand, maintain, defend and enforce our intellectual property portfolio;
- hire additional clinical, regulatory and scientific personnel;
- ultimately establish a sales, marketing and distribution infrastructure to commercialize any products for which we may obtain marketing approval; and
- add operational, legal, compliance, financial and management information systems and personnel to support our research, product development and future commercialization efforts, as well as to support our operations as a public company.

Even if we obtain regulatory approval of, and are successful in commercializing, one or more of our product candidates, we will continue to incur substantial research and development and other costs to develop and market additional product candidates. We may encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may adversely affect our business. The size of our future net losses will depend, in part, on the rate of future growth of our expenses and our ability to generate revenue.

We have never generated revenue from product sales and may never achieve or maintain profitability.

While we have completed our Phase 1 clinical trial for PGN-EDO51 and initiated two Phase 2 clinical trials for PGN-EDO51 as well as an additional Phase 1 clinical trial for PGN-EDODM1 and more recently, a Phase 2 clinical trial for PGN-EDODM1, we expect that it will be many years, if ever, before we have a product candidate ready for commercialization. In December 2024, the FDA issued a clinical hold on the initiation of our Phase 2 CONNECT2 trial of PGN-EDO51 in DMD in the U.S. It is unknown

whether we may be successful in resolving this hold. More recently, Health Canada has requested additional information from us to address safety concerns before any further dose escalation or enrollment of any additional participants at the current dose levels may proceed in our CONNECT1 study of PGN-EDO51. It is unknown whether Health Canada will allow us to dose escalate or enroll additional participants in this study. Moreover, even if we are successful in removing the FDA clinical hold, it is unknown whether the FDA may require the conduct of additional preclinical studies or clinical trials beyond those which we had planned to conduct. To become and remain profitable, we must succeed in developing, obtaining the necessary regulatory approvals for and eventually commercializing a product or products that generate significant revenue. The ability to achieve this success will require us to be effective in a range of challenging activities, including:

- identifying product candidates and completing preclinical development of our product candidates;
- obtaining regulatory clearance to commence clinical trials and initiating and successfully completing such trials;
- obtaining marketing approval for our product candidates;
- manufacturing (or securing third-party manufacturers to manufacture), marketing and selling any products for which we may obtain regulatory approval;
- achieving market acceptance of any products for which we obtain regulatory approval as a viable treatment option; and
- satisfying any post-marketing requirements.

We are only in the preliminary stages of most of these activities. We may never succeed in these activities and, even if we do, may never generate revenues that are significant enough to achieve profitability. Because of the numerous risks and uncertainties associated with product development, we are unable to accurately estimate or know the nature, timing or costs of the efforts that will be necessary to complete the preclinical and clinical development and commercialization of our product candidates or when, or if, we will be able to generate revenues or achieve profitability.

If we are successful in obtaining regulatory approval to market one or more of our product candidates, our revenue will be dependent, in part, upon the size of the markets in the territories for which we gain regulatory approval, the accepted price for the product, the ability to obtain coverage and reimbursement, and whether we own the commercial rights for that territory. If the number of our addressable patients is not as significant as we estimate, the indication approved by regulatory authorities is narrower than we expect, or the treatment population is narrowed by competition, physician choice or treatment guidelines, we may not generate significant revenue from sales of such products, even if approved.

Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable could impair our ability to raise capital, maintain our research and development efforts, expand our business or even continue our operations. A decline in the value of our company could also cause you to lose all or part of your investment.

We will need to raise substantial additional funding. If we are unable to raise capital when needed, we could be forced to delay, scale back or discontinue our product development programs or future commercialization efforts.

We expect our expenses to increase substantially in connection with our ongoing activities, particularly as we identify, continue the research and development of, continue preclinical testing and initiate clinical trials of, arrange for the manufacturing of, and potentially seek marketing approval for any product candidates that successfully completes clinical testing. To date, we have only completed a Phase 1 clinical trial for our first product candidate, PGN-EDO51, initiated one additional Phase 1 clinical trial for PGN-EDODM1, two Phase 2 clinical trials for PGN-EDO51 and more recently, one Phase 2 clinical trial for PGN-EDODM1. The resolution of the clinical hold in the U.S. on the initiation of the Phase 2 CONNECT2 clinical trial of PGN-EDO51, assuming resolution is reached with the FDA, may require additional capital beyond that we had planned to allocate to this program, and the amount of such capital could be considerable. In addition, if we obtain marketing approval for any product candidate, we expect to incur significant commercialization expenses related to product manufacturing, marketing, sales and distribution. Furthermore, we expect to continue to incur additional costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed, on attractive terms or at all, we may be forced to delay, reduce or eliminate our research and development programs or future commercialization efforts.

As of December 31, 2024, we had cash, cash equivalents, and marketable securities of \$120.2 million. Prior to our IPO in May 2022, we raised aggregate gross proceeds of \$133.5 million from the private placement of convertible preferred stock. We raised aggregate gross proceeds of \$122.9 million from our IPO.

On February 5, 2024, we sold shares of common stock under our at-the-market offering program, or ATM program, pursuant to an At-the-Market Equity Offering Sales Agreement, or Sales Agreement, with Stifel, Nicolaus & Company, Incorporated, or Stifel, resulting in net proceeds of \$9.9 million. On February 9, 2024, we sold shares of common stock in an underwritten follow-on

offering, or the Follow-on Offering, resulting in net proceeds of \$76.4 million after deducting underwriters' fees of \$3.7 million. Net proceeds from the ATM program and Follow-on Offering, after deducting underwriters' fees and costs of the offerings, were \$86.3 million.

Based on our currently planned operations, we believe that our existing cash, cash equivalents, marketable securities will be sufficient to fund our operations for at least 12 months from the date of the filing of this 10-K. However, we have based this estimate on assumptions that may prove to be wrong, and our operating plans may change as a result of many factors, including factors currently unknown to us. As a result, we could deplete our capital resources sooner than we currently expect and could be forced to seek additional funding sooner than planned.

Our future capital requirements will depend on many factors, including:

- the scope, progress, costs and results of preclinical and clinical development for our product candidates and any additional product candidates we may develop or any new indications we may pursue;
- the scope, costs, timing and outcome of regulatory review of our product candidates and any additional product candidates we may develop or any new indications we may pursue;
- the cost and timing of manufacturing activities;
- the identification of additional research programs and product candidates;
- the costs and scope of the continued development of our EDO platform;
- the costs and timing of preparing, filing and prosecuting applications for patents, maintaining and enforcing our intellectual property rights and defending any intellectual property-related claims, including claims of infringement, misappropriation or other violations of third-party intellectual property;
- the costs and timing of future commercialization activities, including product manufacturing, marketing, sales and distribution, for any product candidate that receives marketing approval;
- the costs of satisfying any post-marketing requirements;
- the revenue, if any, received from commercial sales of our product candidates if marketing approval is received;
- the costs of operational, financial and management information systems and associated personnel;
- the associated costs in connection with any acquisition of in-licensed products, intellectual property and technologies; and
- the costs of operating as a public company.

Identifying potential product candidates and conducting preclinical testing and clinical trials are time-consuming, expensive and uncertain processes requiring years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve product sales. In addition, even if we successfully develop product candidates and those are approved, we may not achieve commercial success. Our commercial revenues, if any, may not be sufficient to sustain our operations. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms, or at all.

Any additional fundraising efforts may divert our management from their day-to-day activities, which may adversely affect our operations. We cannot be certain that additional funding will be available on acceptable terms, when needed or at all. We have no committed source of additional capital and, if we are unable to raise additional capital in sufficient amounts, when needed or on terms acceptable to us, we may be required to significantly curtail, delay or discontinue one or more of our research or development programs or the commercialization of any product candidate, or be unable to expand our operations or otherwise capitalize on our business opportunities, as desired, which could materially affect our business, financial condition and results of operations. We could be required to seek collaborators for product candidates at an earlier stage than otherwise would be desirable or on terms that are less favorable than might otherwise be available or relinquish or license on unfavorable terms our rights to product candidates in markets where we otherwise would seek to pursue development or commercialization ourselves. Any of the above events could significantly harm our business, prospects, financial condition and results of operations and cause the price of our common stock to decline.

Our limited operating history may make it difficult for you to evaluate the success of our business to date and to assess our future viability.

We commenced operations in 2018, have no products approved for commercial sale and have not generated any revenue from product sales. To date, our operations have been limited to organizing and staffing our company, business planning, executing collaborations, raising capital, licensing, conducting research activities, conducting preclinical studies of our programs and clinical trials of our product candidates, filing and prosecuting patent applications and providing general and administrative support for these

operations. One of our product candidates, PGN-EDO51, completed a Phase 1 clinical trial and we have initiated one additional Phase 1 clinical trial for PGN-EDODM1 and two Phase 2 clinical trials for PGN-EDO51 and more recently, a Phase 2 clinical trial for PGN-EDODM1. In December 2024, the FDA issued a clinical hold on the initiation of our Phase 2 CONNECT2 trial of PGN-EDO51 in DMD in the U.S. It is unknown whether we may be successful in resolving this hold. Moreover, even if we are successful in removing the hold, it is unknown whether the FDA may require the conduct of additional preclinical studies or clinical trials beyond those which we had planned to conduct. More recently, Health Canada has requested additional information from us to address safety concerns before any further dose escalation or enrollment of any additional participants at the current dose levels may proceed in our CONNECT1 Phase 2 study of PGN-EDO51 in DMD. It is unknown whether Health Canada will allow us to dose escalate or enroll additional participants in this study. All of our other research programs are still in the research or preclinical stage of development, and their risk of failure is high. We have not yet demonstrated our ability to successfully complete clinical trials consistently, obtain marketing approvals, manufacture product on a commercial scale or arrange for a third party to do so on our behalf, or conduct sales, marketing and distribution activities necessary for successful product commercialization. Consequently, any predictions you make about our future success or viability may not be as accurate as they could be if we had a longer operating history or a history of successfully developing and commercializing products.

Our limited operating history may make it difficult to evaluate our technology and industry and predict our future performance. Our limited history as an operating company makes any assessment of our future success or viability subject to significant uncertainty. We will encounter risks and difficulties frequently experienced by early-stage companies in rapidly evolving fields. If we do not address these risks successfully, our business will suffer.

In addition, as our business grows, we may encounter unforeseen expenses, restrictions, difficulties, complications, delays and other known and unknown factors. We will need to continue to transition from a company with a research focus to a company capable of conducting development activities for multiple product candidates and then to a company supporting commercial activities. We may not be successful in such transitions. If we do not adequately address these risks and difficulties or successfully make such a transition, it could have a material adverse impact on our business.

Risks Related to Discovery, Development, Preclinical and Clinical Testing

We are early in our development efforts. We have only completed a Phase 1 clinical trial for our lead product candidate and initiated several additional clinical trials, and as a result it will be years before we commercialize a product candidate, if ever. If we are unable to advance our product candidates through preclinical studies and clinical trials, obtain marketing approval and ultimately commercialize them, or experience significant delays in doing so, our business will be materially harmed.

We are early in our development efforts and have invested our research efforts to date in developing our EDO platform. We have a portfolio of research programs, and we have two product candidates in clinical trials — PGN-EDO51 for DMD and PGN-EDODM1 for DM1. We have completed a Phase 1 clinical trial for our first product candidate, PGN-EDO51 in HVs. We have initiated our Phase 2 CONNECT1 trial for PGN-EDO51 in Canada and began dosing participants in January of 2024. In July 2024, we reported initial data from the low dose cohort (5 mg/kg) in this trial. Based on this data, we have amended the CONNECT1 study protocol to implement several changes. Following notification of the FDA clinical hold referenced below, Health Canada requested additional information from us to address safety concerns before any further dose escalation or enrollment of any additional participants at the current dose levels may proceed in our CONNECT1 study. It is unknown whether Health Canada will allow us to dose escalate or enroll additional participants in this study. We received clearance from the MHRA to initiate our Phase 2 CONNECT2 trial for PGN-EDO51 in the U.K. In December 2024, the FDA issued a clinical hold on the initiation of the CONNECT2 clinical trial in the U.S. We have initiated a Phase 1 clinical trial, designated FREEDOM, for our second product candidate, PGN-EDODM1, and began dosing participants in December 2023. On February 24, 2025, we reported initial single-dose data for each of the first two cohorts (5 and 10 mg/kg) in the Phase 1 FREEDOM study. We have also opened a Phase 2 clinical trial, FREEDOM2, in Canada and the U.K.

We are evaluating additional product candidates in preclinical studies, but have not completed IND- or CTA-enabling activities for any of our other product candidates or advanced any of our other product candidates into clinical trials. Our ability to generate product revenue, which we do not expect will occur for many years, if ever, will depend heavily on the successful clinical development and eventual commercialization of our product candidates, which may never occur. We currently generate no revenue from sales of any product, and we may never be able to develop or commercialize a marketable product.

Commencing clinical trials in the U.S. is subject to authorization by the FDA of an IND and finalizing the trial design based on discussions with the FDA and other regulatory authorities. In the event that the FDA requires us to complete additional preclinical studies, or we are required to satisfy other FDA or other regulator requests prior to commencing clinical trials, the start of our clinical trials may be delayed. As noted above, in December 2024, we announced that FDA had placed a clinical hold on the initiation of our planned Phase 2 CONNECT2 trial in the U.S. In addition, previously, in May 2023, we announced that FDA had placed a clinical hold on our planned Phase 1 FREEDOM clinical trial of PGN-EDODM1 in the U.S. We submitted a response to the FDA and in

October 2023, we announced that the FDA had lifted the clinical hold, allowing us to initiate FREEDOM in the U.S. Even after initiating FREEDOM in the U.S., the FDA or other regulatory authorities could disagree that we have satisfied their requirements to commence any clinical trial, including our FREEDOM2 study of PGN-EDODM1, or disagree with or change their position on the acceptability of our trial design or the clinical endpoints selected, which may require us to complete additional preclinical studies or clinical trials or impose stricter approval conditions than we currently expect. There are equivalent processes and risks applicable to CTAs in other countries, including Canada and countries in Europe. Moreover, regulatory authorities in other countries could request that we pause dosing or further enrollment in one or more of our ongoing studies based in whole or in part on a clinical hold in the U.S.

Commercialization of our product candidates will require preclinical and clinical development; regulatory approval; manufacturing supply, capacity and expertise; a commercial organization; and significant marketing efforts. The success of our product candidates will depend on many factors, including the following:

- timely and successful completion of preclinical studies, including toxicology studies, biodistribution studies and minimally efficacious dose studies in animals, where applicable;
- regulatory clearance to initiate clinical trials under INDs, CTAs or comparable foreign applications that allow commencement of our planned clinical trials or future clinical trials for our product candidates;
- successful initiation, enrollment and completion of clinical trials, including under the FDA's GCP, GLP, and any additional regulatory requirements from foreign regulatory authorities;
- positive results from our clinical trials that support a finding of safety and effectiveness and an acceptable risk-benefit profile in the intended populations to the satisfaction of the applicable regulatory authorities;
- receipt of marketing approvals from applicable regulatory authorities, including the completion of any required post-marketing studies or trials;
- establishment of arrangements through our own facilities or with third-party manufacturers for clinical supply and, where applicable, commercial manufacturing capabilities;
- establishment, maintenance, defense and enforcement of patent, trademark, trade secret and other intellectual property protection or regulatory exclusivity for our product candidates;
- commercial launch of our product candidates, if approved, whether alone or in collaboration with others;
- acceptance of the benefits and use of our product candidates, including method of administration, if and when approved, by patients, the medical community and third-party payors;
- effective competition with other therapies;
- maintenance of a continued acceptable safety, tolerability and efficacy profile of our product candidates following marketing approval, including acceptable results from any post-approval studies or clinical trials agreed to by us or required by FDA or other regulatory authorities; and
- establishment and maintenance of healthcare coverage and adequate reimbursement by payors.

Many of these factors are beyond our control and if we do not succeed in one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize any product candidates, which would materially harm our business. If we are unable to advance our product candidates to clinical development or successfully complete clinical trials, obtain regulatory approval and ultimately commercialize our product candidates, or experience significant delays in doing so, our business will be materially harmed.

Our approach to the discovery and development of product candidates based on our EDO platform is unproven, and we may not be successful in our efforts to identify, discover or develop potential product candidates.

The success of our business depends upon our ability to identify, develop and commercialize products based on our proprietary EDO platform. Our current product candidates that have been developed through our EDO platform are peptide-conjugated oligonucleotides designed to have a disease-modifying impact on degenerative neuromuscular diseases.

Our lead product candidates are currently in clinical-stage development, while our other product candidates are still in the research or preclinical stage of development and our approach to treating muscle disease is unproven. Our research programs may fail to identify potential product candidates for clinical development for a number of reasons. Our research methodology may be unsuccessful in identifying potential product candidates and our potential product candidates may be shown to have harmful side effects in preclinical in vitro experiments or in vivo animal model studies, or in future clinical studies. In addition, our potential

product candidates may not show promising signals of therapeutic effect in such experiments or studies or they may have other characteristics that may make the product candidates impractical to manufacture, unmarketable or unlikely to receive marketing approval. Further, because all of our development programs are based on our EDO platform, adverse developments with respect to one of our programs may have a significant adverse impact on the actual or perceived likelihood of success and value of our other programs. In addition, we may be negatively impacted by the decision of other companies to discontinue development of products using technology similar to our technology. For example, recently, Sarepta announced that it was discontinuing its SRP-5051 peptide-linked PMO development program, based on the risk-benefit of the program, including some patients experiencing hypomagnesemia even after treatment with SRP-5051 was discontinued, feedback from the FDA, and the evolving therapeutic landscape for DMD.

We have advanced our first two product candidates, PGN-EDO51 and PGN-EDODM1, into the clinic, and have completed a Phase 1 trial of PGN-EDO51 in HVs. However, the positive results we have observed in our preclinical studies and in the completed Phase 1 trial may not be repeated in future clinical trials, including in patients with DMD amenable to an exon-51 skipping approach, and regulatory authorities may disagree with the interpretation of data from our trials.

Although we are advancing our initial programs in DMD and DM1, our EDO platform may fail to yield additional product candidates for clinical development for a number of reasons, including those discussed in these risk factors. In addition:

- we may not be able to assemble sufficient resources to acquire or discover product candidates;
- competitors may develop alternatives that render our potential product candidates obsolete or less attractive;
- potential product candidates we develop may be covered by third parties' patents or other intellectual property rights;
- potential product candidates may, on further study, be shown to have harmful side effects, toxicities or other characteristics that indicate that they are unlikely to be products that will receive marketing approval and achieve market acceptance;
- potential product candidates may not be effective in treating their targeted diseases or disorders;
- the market for a potential product candidate may change so that the continued development of that product candidate is no longer reasonable;
- a potential product candidate may not be capable of being produced in commercial quantities at an acceptable cost, or at all; or
- the regulatory pathway for a potential product candidate may be too complex and difficult to navigate successfully or economically.

If we are unable to identify and discover suitable product candidates for clinical development, this would adversely impact our business strategy and our financial position and share price and could potentially cause us to cease operations.

Drug development is a lengthy and expensive process, and preclinical and clinical testing is uncertain as to the outcome. We may encounter substantial delays in the commencement, enrollment or completion of our clinical trials and may never advance to clinical trials, or we may fail to demonstrate safety and effectiveness to the satisfaction of applicable regulatory authorities, which could prevent us from advancing or commercializing our product candidates on a timely basis, if at all.

The risk of failure in developing product candidates is high. It is impossible to predict when or if any product candidate would prove effective or safe in humans or will receive regulatory approval. Before obtaining marketing approval from regulatory authorities for the sale of any product candidate, we must complete preclinical development, obtain regulatory clearance to commence clinical trials, and then conduct extensive clinical trials to demonstrate the safety and efficacy of product candidates in humans. To date, we have only completed a Phase 1 clinical trial of PGN-EDO51 and initiated an additional Phase 1 clinical trial of PGN-EDODM1, two Phase 2 clinical trials of PGN-EDO51 and more recently, a Phase 2 clinical trial of PGN-EDODM1.

Clinical trials may fail to demonstrate that our product candidates are safe for humans and effective for indicated uses, and earlier results, both preclinical and clinical, may not be indicative of future clinical trial results. Even if the clinical trials are successful, changes in marketing approval policies during the development period, changes in or the enactment or promulgation of additional statutes, regulations or guidance, varying interpretations of clinical data or changes in regulatory review for each submitted product application may cause delays in the approval or rejection of an application.

Before we can commence clinical trials for a product candidate, we must complete extensive preclinical testing and studies that support clearance of our INDs, CTAs and other similar regulatory filings. We cannot be certain if the outcome of our preclinical studies and clinical trials will ultimately support further development of our product candidates or future programs, or future regulatory approval and commercialization. Although we have completed a Phase 1 study of our lead product candidate, PGN-EDO51, initiated two Phase 2 studies of PGN-EDO51 and initiated an additional Phase 1 and a Phase 2 clinical trial of our second candidate, PGN-EDODM1, we cannot be certain of the completion or outcome of our preclinical testing and studies for our other

product candidates and cannot predict whether the FDA, European Medicines Agency, or EMA, or comparable foreign regulatory authorities will accept our proposed clinical programs for PGN-EDO51 or PGN-EDODM1, or whether the outcome of our preclinical testing and studies will ultimately support the further development of our other product candidates. For example, Health Canada has recently requested additional information from us to address safety concerns before any further dose escalation or enrollment of any additional participants at the current dose levels may proceed in our Phase 2 CONNECT1 study of PGN-EDO51 in DMD. It is unknown whether Health Canada will allow us to dose escalate or enroll additional participants in this study. In addition, in December 2024, the FDA issued a clinical hold on the initiation of our Phase 2 CONNECT2 trial of PGN-EDO51 in DMD planned to be initiated in the U.S. It is unknown whether we may be successful in resolving this hold. Moreover, even if we are successful in removing the hold, it is unknown whether the FDA may require the conduct of additional preclinical studies or clinical trials beyond those which we are conducting or plan to conduct. Conducting preclinical testing is a lengthy, time-consuming and expensive process. The length of time may vary substantially according to the type, complexity and novelty of the program, and often can be several years or more per program. In addition, the progress and timing of our preclinical studies, including pharmacology and toxicology studies, may be impacted by the limited supply of NHPs needed for such studies. As a result, we cannot be sure that we will be able to submit INDs, CTAs and other similar regulatory filings for our programs on the timelines we expect, if at all, and we cannot be sure that submission of such regulatory filings will result in the FDA, EMA or comparable foreign regulatory authorities allowing clinical trials to begin, including in the case of our CONNECT2 clinical study for PGN-EDO51 and our FREEDOM2 clinical study for PGN-EDODM1. For example, in May 2023, we announced that we received a clinical hold notice from the FDA regarding our IND application to initiate our Phase 1 FREEDOM study, and in June 2023, we provided an update on our plans with respect to this program. In October 2023, we announced that the FDA lifted the clinical hold on our Phase 1 FREEDOM study, allowing this study to proceed in the U.S.

Furthermore, product candidates are subject to continued preclinical safety studies, which may be conducted concurrently with our clinical testing. The outcomes of these safety studies may delay the launch of, or enrollment in clinical trials and could impact our ability to continue to conduct our clinical trials.

Clinical testing is expensive, is difficult to design and implement, can take many years to complete and is uncertain as to outcome. We cannot guarantee that any clinical trials will be conducted as planned or completed on schedule, or at all. A failure of one or more clinical trials can occur at any stage of testing, which may result from a multitude of factors, including, but not limited to, flaws in trial design, dose selection issues, patient enrollment criteria and failure to demonstrate favorable safety or efficacy traits. Other events that may prevent successful or timely completion of clinical development include:

- delays in reaching a consensus with regulatory authorities on trial design;
- delays in reaching agreement on acceptable terms with prospective clinical research organizations, or CROs, and clinical trial sites;
- delays in opening clinical trial sites or obtaining required IRB, or independent ethics committee approval, or the equivalent review groups for sites outside the U.S., at each clinical trial site;
- imposition of a clinical hold by regulatory authorities as a result of a serious adverse event or manufacturing concerns or after an inspection of our clinical trial operations or trial sites;
- negative or inconclusive results observed in clinical trials, including failure to demonstrate statistical significance, which could lead us, or cause regulators to require us, to conduct additional clinical trials or abandon product development programs;
- failure by us, any CROs we engage or any other third parties to adhere to clinical trial requirements;
- failure to perform in accordance with the FDA's GCPs or those of other regulatory authorities;
- failure by physicians to adhere to delivery protocols leading to variable results;
- delays in the testing, validation, manufacturing and delivery of our product candidates to the clinical sites, including delays by third parties with whom we have contracted to perform certain of those functions;
- failure of our third-party contractors to comply with regulatory requirements or to meet their contractual obligations to us in a timely manner, or at all;
- inability to recruit patients to participate in a clinical trial, including as a result of competition with other pharmaceutical and biotechnology companies and the patient population size for our product candidates;
- delays in having patients complete participation in a clinical trial or return for post-treatment follow-up;
- clinical trial sites or patients dropping out of a trial;
- selection of clinical endpoints that require prolonged periods of clinical observation or analysis of the resulting data;

- occurrence of serious adverse events associated with the product candidate that are viewed to outweigh its potential benefits;
- occurrence of serious adverse events associated with a product candidate in development by another company, which are viewed to outweigh its potential benefits, and which may negatively impact the perception of our product due to a similarity in technology or approach;
- changes in regulatory requirements and guidance that require amending or submitting new clinical protocols;
- changes in the legal or regulatory regimes domestically or internationally related to patient rights and privacy;
- lack of adequate funding to continue the clinical trial; or
- lack of diminished revenue potential of the program(s) due to competition.

Clinical trials must be conducted in accordance with the FDA and other applicable regulatory authorities' legal requirements, regulations or guidelines, and are subject to oversight by these governmental agencies and IRBs or ethics committees at the medical institutions where the clinical trials are conducted. We could encounter delays if a clinical trial is suspended or terminated by us, by the DSMB for such trial or by the FDA or any other regulatory authority, or if the IRBs of the institutions in which such trials are being conducted suspend or terminate the participation of their clinical investigators and sites subject to their review. Such authorities may suspend or terminate a clinical trial due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a product candidate, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial.

In addition, disruptions caused by the effects of any epidemics or pandemics may increase the likelihood that we encounter such difficulties or delays in initiating, enrolling, conducting or completing our planned and ongoing clinical trials.

Moreover, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and receive compensation in connection with such services. Under certain circumstances, we may be required to report some of these relationships to the FDA or comparable foreign regulatory authorities. The FDA or comparable foreign regulatory authority may conclude that a financial relationship between us and a principal investigator has created a conflict of interest or otherwise affected interpretation of the trial. The FDA or comparable foreign regulatory authority may therefore question the integrity of the data generated at the applicable clinical trial site and the utility of the clinical trial itself may be jeopardized. This could result in a delay in approval, or rejection, of our marketing applications by the FDA or comparable foreign regulatory authority, as the case may be, and may ultimately lead to the denial of marketing approval of our product candidates.

Any inability to successfully complete preclinical studies and clinical trials could result in additional costs to us or impair our ability to generate revenues from product sales, regulatory and commercialization milestones and royalties. In addition, if we make manufacturing or formulation changes to our product candidates, we may need to conduct additional studies to bridge our modified product candidates to earlier versions. Clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do, which could impair our ability to successfully commercialize our product candidates and may harm our business, financial condition, results of operations and prospects.

Further, conducting clinical trials in foreign countries, as we plan to continue to do for our product candidates, presents additional risks that may delay completion of our clinical trials. These risks include the failure of enrolled patients in foreign countries to adhere to clinical protocol as a result of differences in healthcare services or cultural customs, managing additional administrative burdens associated with foreign regulatory schemes, as well as political and economic risks relevant to such foreign countries. Additionally, if the results of clinical trials are inconclusive or if there are safety concerns or serious adverse events associated with our product candidates, we may:

- be delayed in obtaining marketing approval for product candidates, if at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or safety warnings;
- be subject to changes in the way the product is administered;
- be required to perform additional clinical trials to support approval or be subject to additional post-marketing testing requirements;
- have regulatory authorities withdraw, or suspend, their approval of the product or impose restrictions on its distribution in the form of a REMS;

- be subject to the addition of labeling statements, such as warnings or contraindications;
- be sued; or
- experience damage to our reputation.

In particular, each of the conditions for which we plan to develop or are developing product candidates is a rare genetic disease with limited patient pools from which to draw for clinical trials. Further, because it can be difficult to diagnose these diseases in the absence of a genetic screen, we may have difficulty finding patients who are eligible to participate in our studies. The eligibility criteria of our clinical trials will further limit the pool of available study participants. Additionally, the process of finding and diagnosing patients may prove costly. The treating physicians in our clinical trials may also use their medical discretion in advising patients enrolled in our clinical trials to withdraw from our studies or to try alternative therapies. Finally, we must compete with other companies with either approved therapies or investigational therapies in development for the conditions which we are developing product candidates for, which may further limit the pool of potential patients.

The outcome of preclinical studies and earlier-stage clinical trials may not be predictive of future results or the success of later preclinical studies and clinical trials.

We are in the early stages of our programs and have successfully completed a Phase 1 HV clinical trial in Canada for our lead product candidate, PGN-EDO51, reported early data from the low dose cohort of our first Phase 2 trial of PGN-EDO51 in DMD patients, initiated Phase 1 and Phase 2 clinical trials for our PGN-EDODM1 product candidate and reported initial data from the first two cohorts of our Phase 1 trial of PGN-EDODM1, but we have not completed IND- or CTA-enabling activities for our other product candidates or advanced any other product candidates into clinical development. As a result, our belief in the capabilities of our platform is based on early research, preclinical studies, our completed Phase 1 clinical trial in HVs and early data from our Phase 2 study of PGN-EDO51 and our Phase 1 study of PGN-EDODM1. However, the results of preclinical studies may not be predictive of the results of later preclinical studies or clinical trials, and the results of any early-stage clinical trials may not be predictive of the results of later clinical trials. For example, we may not see the same levels of exon skipping, oligonucleotide delivery or dystrophin production in DMD patients as was observed in our preclinical studies or, with respect to exon skipping and oligonucleotide delivery, in our Phase 1 HV study of PGN-EDO51. While we saw high mean levels of exon skipping (2.15%) in all participants at the 5 mg/kg starting dose of our CONNECT1 Phase 2 study after four doses and three months of treatment, we did not achieve the level of dystrophin that we had anticipated. With a longer treatment period and higher doses of PGN-EDO51, we expect to see higher levels of exon skipped transcript potentially resulting in significant increases in dystrophin, but this may not be the case. Given Health Canada's recent request for additional information from us to address safety concerns before any further dose escalation or enrollment of any additional participants at the current dose levels may proceed in our CONNECT1 study, we may be unable to further advance the CONNECT1 study beyond dosing of the currently enrolled participants at current dose levels. In addition, with the current clinical hold on initiation of our CONNECT2 clinical trial in the U.S. for PGN-EDO51 in DMD, we may be unable to advance development of PGN-EDO51 for DMD in the U.S. On February 24, 2025, we reported initial single-dose data for each of the first two cohorts (5 and 10 mg/kg) in the Phase 1 FREEDOM study. While we observed robust and dose-dependent mean splicing correction (29.1%) at the 10 mg/kg dose level, we observed limited change in functional outcomes after a single dose over one month. We believe robust splicing correction with PGN-EDODM1 has the potential to lead to meaningful functional improvements with repeat dosing over time, but this may not be the case. Initial success in clinical trials, including in our CONNECT1 and FREEDOM studies, may not be indicative of results obtained when such trials are completed. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their products. Our clinical trials may not ultimately be successful or support further clinical development of our product candidates. There is a high failure rate for product candidates proceeding through clinical trials. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in clinical development even after achieving encouraging results in earlier studies. Any such setbacks in our clinical development could materially harm our business and results of operations.

Additionally, our planned clinical trials may utilize an "open-label" trial design. An "open-label" clinical trial is one where both the patient and investigator know whether the patient is receiving the investigational product candidate or either an existing approved drug or placebo. Most typically, open-label clinical trials test only the investigational product candidate and sometimes may do so at different dose levels. Open-label clinical trials are subject to various limitations that may exaggerate any therapeutic effect as patients in open-label clinical trials are aware when they are receiving treatment. Open-label clinical trials may be subject to a "patient bias" where patients perceive their symptoms to have improved merely due to their awareness of receiving an experimental treatment. In addition, open-label clinical trials may be subject to an "investigator bias" where those assessing and reviewing the physiological outcomes of the clinical trials are aware of which patients have received treatment and may interpret the information of the treated group more favorably given this knowledge. The results from an open-label trial may not be predictive of future clinical trial results with any of our product candidates when studied in a controlled environment with a placebo or active control.

If we experience delays or difficulties in the enrollment of patients in clinical trials, our ability to complete clinical trials may be adversely impacted.

Identifying and qualifying patients to participate in clinical trials of our product candidates is critical to our success. We may not be able to identify, recruit and enroll a sufficient number of patients, or those with required or desired characteristics, to complete our clinical trials in a timely manner. Patient enrollment and trial completion is affected by factors including:

- perceived risks and benefits of novel unproven approaches;
- size of the patient population, in particular for rare diseases such as the diseases on which we are initially focused, and process for identifying patients;
- design of the trial protocol;
- eligibility and exclusion criteria;
- perceived risks and benefits of the product candidate under study;
- availability of competing therapies and clinical trials;
- severity of the disease or disorder under investigation;
- proximity and availability of clinical trial sites for prospective patients;
- ability to obtain and maintain patient consent;
- risk that enrolled patients will drop out before completion of the trial;
- ability to recruit clinical trial investigators of appropriate competencies and experience;
- patient referral practices of physicians;
- ability to monitor patients adequately during and after treatment; and
- other factors outside of our control, such as the potential effects of any epidemics, pandemics or health crisis.

For example, DMD amenable to exon 51 skipping is a rare disease, and there are several therapies approved in certain territories or in clinical development, which can make enrollment in our CONNECT1 and CONNECT2 trials more challenging. Our inability to enroll a sufficient number of patients for our clinical trials, including our ongoing trials for PGN-EDO51 and PGN-EDODM1, would result in significant delays and could require us to abandon one or more clinical trials altogether. Enrollment delays in these clinical trials may result in increased development costs for our product candidates, which would cause the value of our company to decline and limit our ability to obtain additional financing. Furthermore, we rely on and expect to continue to rely on CROs and clinical trial sites to ensure the proper and timely conduct of our clinical trials and we will have limited influence over their performance.

Even if we are able to enroll a sufficient number of patients for our clinical trials, we may have difficulty maintaining patients in our clinical trials. Many of the patients who end up receiving placebo may perceive that they are not receiving the product candidate being tested, and they may decide to withdraw from our clinical trials to pursue other alternative therapies rather than continue the trial with the perception that they are receiving placebo. If we have difficulty enrolling or maintaining a sufficient number of patients to conduct our clinical trials, we may need to delay, limit or terminate clinical trials, any of which would harm our business, financial condition, results of operations and prospects.

Interim, initial, “topline”, and preliminary data from our preclinical studies or clinical trials that we announce or publish from time to time may change as more patient 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 publicly disclose preliminary or topline data from our preclinical studies and 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 study or trial. For example, in September 2022, we announced results from our Phase 1 clinical trial of PGN-EDO51, in July 2024, we announced initial results from our CONNECT1 Phase 2 trial from the low dose (5 mg/kg) cohort as well as high level safety information for the ongoing 10 mg/kg dose cohort, and more recently, we provided additional safety information from the ongoing CONNECT1 trial. On February 24, 2025, we announced initial results from our FREEDOM Phase 1 trial from the 5 and 10 mg/kg dose cohorts. The topline or preliminary 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. Topline data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, topline data and preliminary results should be viewed with caution until the final data are available.

From time to time, we may also disclose interim data from our preclinical studies and clinical trials. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available or as patients from our clinical trials continue other treatments for their disease. Adverse differences between preliminary or interim data and final data could significantly harm our business prospects. Further, disclosure of interim data could result in volatility in the price of our common stock.

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 material or otherwise appropriate information to include in our disclosure.

If the interim, topline, or preliminary 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, our product candidates may be harmed, which could harm our business, operating results, prospects or financial condition.

If any of our product candidates cause undesirable side effects or have other unexpected adverse properties, such side effects or properties could delay or prevent the initiation or completion of clinical trials, regulatory approval, limit the commercial potential or result in significant negative consequences following any potential marketing approval.

We have completed dosing up to 15 mg/kg in a Phase 1 clinical trial of PGN-EDO51, in which PGN-EDO51 was observed to be generally well-tolerated in HVs at clinically active doses, and are dosing participants at 5 mg/kg and 10 mg/kg in an ongoing Phase 2 clinical trial of PGN-EDO51, in which we believe PGN-EDO51 has continued to demonstrate a favorable safety profile as of January 23, 2025, but there can be no assurance that our product candidates will not cause undesirable side effects in patients. For example, in preclinical toxicology studies of PGN-EDO51 in normal NHPs, we observed transient, clinical signs of hypotension in some animals treated at a dose level higher than that which we intend to evaluate in the clinic. In addition, in our Phase 1 clinical trial of PGN-EDO51, at 15 mg/kg, we observed mild, transient, reversible changes in kidney biomarkers that resolved without intervention in all but one participant who experienced a non-life threatening serious adverse event. While the trial was not halted by the safety review committee nor put on hold by Health Canada, under the protocol for this Phase 1 clinical trial, any non-life-threatening SAE was considered a DLT. This participant was admitted to the hospital for less than 24 hours, received intravenous hydration, and then was re-admitted to the Phase 1 unit and completed the study. We also observed transient mild to moderate hypomagnesemia in two participants in the Phase 1 trial, which did not require intervention. Based on published data and other publicly available information, such adverse events are consistent with the types of events reported with this class of oligonucleotides in general. In the ongoing CONNECT1 Phase 2 study, based on the totality of data in both the 5 mg/kg cohort and the ongoing 10 mg/kg cohort as of January 23, 2025, we continue to believe PGN-EDO51 has a favorable emerging safety profile. Magnesium levels in two of the participants in the 10 mg/kg cohort, who were previously reported as having asymptomatic hypomagnesemia, have returned to levels within normal limits with administration of ongoing low-dose oral magnesium supplementation. Dosing of one of these two participants was paused due to a reduction of his eGFR. This event did not meet the pre-specified criteria for a DLT. A subsequent nuclear scan indicated measured glomerular filtration rate was in the normal range. The participant's eGFR is improving and the investigator is evaluating for the resumption of dosing as this value returns to baseline levels. We are continuing to review the event and associated potential confounding factors to better understand its manifestation. There have been no treatment-related SAEs, and all treatment-related adverse events have been mild. There was no sustained elevation in kidney biomarkers. There were also no cases of hypokalemia, anemia or thrombocytopenia. We have received communication from Health Canada that dosing of participants in the 5 and 10 mg/kg cohorts may continue at their current dose levels. Health Canada has requested additional information from us to address its safety concerns before any further dose escalation or enrollment of any additional participants at the current dose levels.

On February 24, 2025, we reported initial data from the 5 and 10 mg/kg dose cohorts in our FREEDOM Phase 1 study in DM1 patients. We believe PGN-EDODM1 has a favorable emerging safety profile. Through the data cutoff date of December 3, 2024, PGN-EDODM1 was observed to be generally well-tolerated, with most TEAEs being mild or moderate in severity. There were no adverse events related to electrolytes or renal biomarkers. There can be no assurance that PGN-EDODM1 will not cause undesirable side effects in patients with further dosing and dose escalation, including safety events similar to those observed in our studies with PGN-EDO51.

Although other oligonucleotide therapeutics have received regulatory approval, ours is a novel approach to oligonucleotide therapy. As a result, there is uncertainty as to the safety profile of our product candidates compared to more well-established classes of therapies, or oligonucleotide therapeutics on their own. Moreover, there have been only a limited number of clinical trials involving the use of peptide conjugated oligonucleotide therapeutics and only one completed trial involving the proprietary technology used in our EDO platform.

Despite the outcome of our Phase 1 clinical trial of PGN-EDO51 and the early results from our Phase 2 CONNECT1 study, as well as the initial results from our Phase 1 clinical trial of PGN-EDODM1, further results from our CONNECT1 or FREEDOM trials or future results from our CONNECT2 Phase 2 clinical trials for PGN-EDO51 or our FREEDOM2 Phase 2 clinical trial of PGN-EDODM1, or studies of any other product candidate could reveal a high and unacceptable severity and prevalence of side effects or

unexpected characteristics than previously anticipated. If any product candidates we develop are associated with serious adverse events, undesirable side effects or unexpected characteristics, we may need to abandon their development or limit development to certain uses or subpopulations in which the serious adverse events, undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective, any of which would have a material adverse effect on our business, financial condition, results of operations and prospects. In addition, regulatory authorities may draw different conclusions, require additional testing to confirm these determinations, require more restrictive labeling or deny regulatory approval of the product candidate. Many product candidates that initially showed promise in early-stage testing have later been found to cause side effects that prevented further clinical development of the product candidates.

It is possible that, as we test our product candidates in larger, longer and more extensive clinical trials, including with different dosing regimens, or as the use of our product candidates becomes more widespread following any regulatory approval, illnesses, injuries, discomforts and other adverse events that were observed in earlier trials, as well as conditions that did not occur or went undetected in previous trials, will be reported by patients. If such side effects become known later in development or upon approval, if any, such findings may harm our business, financial condition, results of operations and prospects significantly.

In addition, if our product candidates receive marketing approval, and we or others later identify undesirable side effects caused by treatment with such drug, a number of potentially significant negative consequences could result, including:

- regulatory authorities may suspend, limit or withdraw approvals of such product, or seek an injunction against its manufacture or distribution;
- we may be required to recall a product or change the way the drug is administered to patients;
- regulatory authorities may require additional warnings in the labeling, such as a contraindication or a boxed warning, 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 change the way the product is administered or conduct additional clinical trials or post-approval studies;
- we may be required to implement a REMS, or create a medication guide outlining the risks of such side effects for distribution to patients;
- additional restrictions may be imposed on the marketing or promotion of the particular product or the manufacturing processes for the product or any component thereof;
- we may be subject to fines, injunctions or the imposition of criminal penalties;
- we could be sued and held liable for harm caused to patients;
- the drug could become less competitive; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of our lead product candidate or our other product candidates, if approved, and could significantly harm our business, financial condition, results of operations and prospects.

We may expend our limited resources to pursue a particular program, product candidate or indication and fail to capitalize on programs, product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and managerial resources, we focus on research programs and expect to focus on product candidates that we identify for specific indications among many potential options. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential, or we may choose to focus our efforts and resources on a potential product candidate that ultimately proves to be unsuccessful. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable medicines. 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 royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate. Any such event could have a material adverse effect on our business, financial condition, results of operations and prospects.

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

Social media is increasingly being used to communicate about pharmaceutical companies' clinical development activities, and we intend to utilize appropriate social media in connection with our development efforts. Additionally, patients may use social media channels to comment on their experience in an ongoing blinded clinical trial or to report an alleged adverse event. If such disclosures occur in the future in connection with any of our sponsored clinical trials, there is a risk that trial enrollment may be adversely impacted, that we may fail to monitor and comply with applicable adverse event reporting obligations or that we may not be able to defend our business or the public's legitimate interests in the face of the political and market pressures generated by social media due to restrictions on what we may say about our product candidates. There is also a risk of inappropriate disclosure of sensitive or confidential information or negative or inaccurate posts or comments about us on any social networking website. In addition, we may encounter attacks on social media regarding our company, management or our product candidates, and fraudsters could and have attempted to illegally use our name on social media platforms to defraud the public. It is also possible for individuals or groups to target companies with disruptive social media campaigns related to a request for access to unapproved drugs for patients with significant unmet medical need. If we experience a similar social media campaign regarding our decision to provide or not provide access to any of our product candidates under an expanded access policy, our reputation may be negatively affected and our business may be harmed. If any of these events were to occur or we fail to comply with applicable regulations, we could incur liability, face regulatory actions or incur other harm to our business.

Clinical trial and product liability lawsuits against us could divert our resources, could cause us to incur substantial liabilities and could limit commercialization of our product candidates.

We face an inherent risk of clinical trial and product liability exposure related to the testing of product candidates that have entered or eventually proceed to clinical trials, and we will face an even greater risk if we commercially sell any products that receive marketing approval. While we currently have only two product candidates in clinical development and none that have been approved for commercial sale, the future use of product candidates by us in clinical trials, and the sale of any approved products in the future, may expose us to liability claims. These claims might be made by patients that use the product, healthcare providers, pharmaceutical companies or others selling such products. If we cannot successfully defend ourselves against claims that our product candidates or products caused injuries, we may incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for our product candidates;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- significant costs to defend any related litigation;
- substantial monetary awards to trial participants or patients;
- loss of revenue;
- reduced resources of our management to pursue our business strategy; and
- the inability to commercialize our product candidates.

We have insurance coverage in place that we believe to be appropriate for our current phase of clinical development, but we may need to further increase this coverage for subsequent clinical trials, or if we commence commercialization of any product candidates. 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 liability that may arise. If a successful clinical trial or product liability claim or series of claims is brought against us for uninsured liabilities or in excess of insured liabilities, our assets may not be sufficient to cover such claims and our business operations could be impaired.

We intend to conduct certain clinical trials for our product candidates outside of the U.S. However, the FDA and comparable foreign regulatory authorities may not accept data from such trials, in which case our development plans will be delayed, which could materially harm our business.

We conducted our first clinical trial in Canada, and we intend to conduct one or more of our subsequent clinical trials for our product candidates outside the U.S., including our ongoing CONNECT1 Phase 2 trial in Canada, and our ongoing CONNECT2, FREEDOM and FREEDOM2 clinical trials, each of which has or will have sites in multiple countries outside of the U.S. Although the FDA may accept data from clinical trials conducted outside the U.S., acceptance of this data is subject to certain conditions imposed by the FDA. Where data from foreign clinical trials are intended to serve as the basis for marketing approval in the U.S., the FDA will not approve the application on the basis of foreign data alone unless those data are applicable to the U.S. population and U.S. medical practice; the studies were performed by clinical investigators of recognized competence; and the data are considered valid without the

need for an on-site inspection by the FDA or, if the FDA considers such an inspection to be necessary, the FDA is able to validate the data through an on-site inspection or other appropriate means. For studies that are conducted only at sites outside of the U.S. and not subject to an IND, the FDA generally does not provide advance comment on the clinical protocols for the studies, and therefore there is an additional potential risk that the FDA could determine that the study design or protocol for a non-U.S. clinical trial was inadequate, which could require us to conduct additional clinical trials. In addition, even where the foreign study data are not intended to serve as the sole basis for approval, the FDA will not accept the data as support for an application for marketing approval unless the study is well-designed and well-conducted in accordance with GCP and the FDA is able to validate the data from the study through an onsite inspection if deemed necessary. Many foreign regulatory authorities have similar approval requirements. There can be no assurance the FDA will accept data from clinical trials conducted outside of the U.S. If the FDA does not accept data from our clinical trials of our product candidates, it would likely result in the need for additional clinical trials, which would be costly and time consuming and delay or permanently halt our development of our product candidates.

Conducting clinical trials outside the U.S. also exposes us to additional risks, including risks associated with:

- additional foreign regulatory requirements;
- foreign exchange fluctuations;
- compliance with foreign manufacturing, customs, shipment and storage requirements;
- cultural differences in medical practice and clinical research; and
- diminished protection of intellectual property in some countries.

Risks Related to Our Dependence on Third Parties

We rely, and expect to continue to rely, on third parties to conduct some or all aspects of our product manufacturing, research and preclinical and clinical testing, and these third parties may not perform satisfactorily.

We do not expect to independently conduct all aspects of our product manufacturing, research and preclinical and clinical testing. We currently rely, and expect to continue to rely, on third parties with respect to many of these items, including CDMOs, for the manufacturing of any product candidates we test in preclinical or clinical development, as well as CROs for the conduct of our animal testing and research and for the conduct of our current and planned clinical trials. Any of these third parties may terminate their engagements with us at any time. If we need to enter into alternative arrangements, it could delay our product development activities.

Our reliance on these third parties for research and development activities will reduce our control over these activities but will not relieve us of our responsibility to ensure compliance with all required regulations and study protocols. For example, we will remain responsible for ensuring that each of our IND- and CTA-enabling studies and clinical trials are conducted in accordance with the study plan and protocols. Moreover, the FDA requires us to comply with GCPs for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. We also are required to register ongoing clinical trials and post the results of completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within specified timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions. If we or any of our CROs or other third parties, including trial sites, fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA, EMA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials complies with GCP regulations. In addition, our clinical trials must be conducted with product produced under conditions that comply with the FDA's cGMPs. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process.

Although we intend to design the preclinical studies and clinical trials for our product candidates, CROs will conduct some or all of the preclinical studies and clinical trials. As a result, many important aspects of our development programs, including their conduct and timing, will be outside of our direct control. Our reliance on third parties to conduct future preclinical studies and clinical trials will also result in less direct control over the management of data developed through preclinical studies and clinical 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 as well as difficulties in coordinating activities. Outside parties may:

- have staffing difficulties;
- fail to comply with contractual obligations;
- experience regulatory compliance issues;
- undergo changes in priorities or become financially distressed; or

- form relationships with other entities, some of which may be our competitors.

These factors may materially adversely affect the willingness or ability of third parties to conduct our preclinical studies and clinical trials and may subject us to unexpected cost increases that are beyond our control. In addition, any third parties conducting our clinical trials will not be our employees, and except for remedies available to us under our agreements with such third parties, we cannot control whether or not they devote sufficient time and resources to our clinical programs. If the CROs and other third parties do not perform preclinical studies and clinical trials in a satisfactory manner, if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols, or if they breach their obligations to us or fail to comply with regulatory requirements, the development, regulatory approval and commercialization of our product candidates may be delayed, we may not be able to obtain regulatory approval and commercialize our product candidates or our development programs may be materially and irreversibly harmed. If we are unable to rely on preclinical and clinical data collected by our CROs and other third parties, we could be required to repeat, extend the duration of or increase the size of any preclinical studies or clinical trials we conduct and this could significantly delay commercialization and require greater expenditures.

If third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our studies in accordance with regulatory requirements or our stated study plans and protocols, we will not be able to complete, or may be delayed in completing, the preclinical studies and clinical trials required to support future IND, CTA and other similar regulatory filings and potential approval of our product candidates.

In addition, there are few CDMOs that have the capability to manufacture oligonucleotides and peptides, the key intermediates in the synthesis of the final active pharmaceutical ingredient, both of which are critical to the development and production of our product candidates. We are aware that one or more of our competitors are using either oligonucleotides, peptides, or both in their product candidates, and that they have engaged with many of these CDMOs, which may hinder our ability to also contract with those CDMOs. As a result, we may have difficulty finding and engaging sufficient third-party manufacturers to develop and manufacture our product candidates, which may affect our ability to conduct preclinical studies and clinical trials. Moreover, legislative proposals are pending that, if enacted, could negatively impact U.S. funding for certain biotechnology providers, including some of our vendors, that may have relationships with certain foreign governments or are viewed as posing a threat to national security. If certain of these vendors are unable to continue to provide services or we are unable to contract with such vendors, this could further constrain our ability to find and engage third-party manufacturers to develop and manufacture our product candidates, which could adversely affect our business.

We currently depend on a small number of third-party suppliers to supply the product candidates that we are evaluating in our research programs. The loss of these or future third-party suppliers, or their inability to provide us with sufficient supply, could harm our business.

We do not own or operate manufacturing facilities and have no current plans to develop our own clinical or commercial-scale manufacturing capabilities. We rely on a small number of third-party suppliers for the manufacture of the product candidates that we are evaluating in our research programs. We expect to continue to depend on third-party suppliers for the manufacture of any product candidates we advance into preclinical and clinical development, as well as for commercial manufacture if those product candidates receive marketing approval. The facilities used by third-party manufacturers to manufacture our product candidates must be approved by the FDA, the EMA and any comparable foreign regulatory authority pursuant to inspections that will be conducted after we submit an NDA to the FDA or any comparable filing to the EMA or other foreign regulatory authority. We do not control the manufacturing process of, and are completely dependent on, third-party manufacturers for compliance with cGMP requirements for the manufacture of products. If these third-party manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA, the EMA or any comparable foreign regulatory authority, we may incur delays in our clinical trials or regulatory submissions, and 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 third-party manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA, the EMA or any comparable foreign regulatory authority does not approve these facilities for the manufacture of our 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 our product candidates, if approved. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, seizures or recalls of product candidates or products, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our product candidates.

We may also seek to eventually establish our own manufacturing facility for the long-term commercial supply of our product candidates for which receive regulatory approval, if any. If we determine to establish our own manufacturing facility and manufacture our products on our own, we will need to obtain the resources and expertise in order to build such manufacturing capabilities and to conduct such manufacturing operations. In addition, our conduct of such manufacturing operations will be subject to the extensive

regulations and operational risks to which our third-party suppliers are subject. If we are not successful in building these capabilities or complying with the regulations or otherwise operating our manufacturing function, our commercial supply could be disrupted and our business could be materially harmed.

Our or a third party's failure to execute on our manufacturing requirements on commercially reasonable terms and in compliance with cGMP could adversely affect our business in a number of ways, including:

- an inability to initiate or conduct preclinical studies or clinical trials of product candidates;
- delays in initiating or completing preclinical studies or clinical trials of product candidates or in submitting regulatory applications, or receiving marketing approvals, for product candidates;
- subjecting third-party manufacturing facilities or our manufacturing facilities to additional inspections by regulatory authorities;
- requirements to cease development or to recall batches of product candidates; and
- in the event of approval to market and commercialize any product, an inability to meet commercial demands for the product.

We are party to manufacturing agreements with a number of third-party manufacturers. We may be unable to maintain these agreements or establish any additional agreements with third-party manufacturers or to do so on acceptable terms. Even if we are able to maintain or establish agreements with third-party manufacturers, reliance on third-party manufacturers entails additional risks, including:

- failure of third-party manufacturers to comply with regulatory requirements and maintain quality assurance;
- breach of the manufacturing agreement by the third party;
- failure to manufacture according to our specifications;
- failure to manufacture according to our schedule or at all;
- misappropriation of our proprietary information, including our trade secrets and know-how; and
- termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us.

We compete with third parties for access to manufacturing facilities, in particular for the manufacture of oligonucleotides. There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us.

We do not currently have arrangements in place for redundant supply or a second source for all required raw materials. If our existing or future third-party manufacturers cannot perform as agreed, we may be required to replace such manufacturers and we may be unable to replace them on a timely basis or at all.

Additionally, if supply from one approved manufacturer is interrupted, there could be a significant disruption in supply. An alternative manufacturer would need to be qualified and authorized pursuant to a submission to our approved NDA or NDA supplement which could result in further delay. Further, we will also need to verify, such as through comparability or bridging studies, that any new or modified manufacturing processes will produce our product candidate according to the specifications previously submitted to the FDA, the EMA or comparable foreign regulatory authorities. The delays associated with the verification of a new third-party manufacturer could negatively affect our ability to develop product candidates or commercialize our products in a timely manner or within budget. Furthermore, a third-party manufacturer may possess technology related to the manufacture of our product candidate that such third-party manufacturer owns independently. This would increase our reliance on such third-party manufacturer or require us to obtain a license from such third-party manufacturer in order to have another third-party manufacturer manufacture our product candidates. We may be unsuccessful in demonstrating the comparability of clinical supplies to those previously allowed into clinical development by the FDA, the EMA or comparable foreign regulatory authorities which could require the conduct of additional studies or clinical trials.

Switching manufacturers may involve substantial costs and is likely to result in a delay in our desired clinical and commercial timelines. These factors could cause the delay of clinical trials, regulatory submissions, required approvals or commercialization of our product candidates, cause us to incur higher costs and prevent us from commercializing our products successfully. Furthermore, if our suppliers fail to meet contractual requirements, and we are unable to secure one or more replacement suppliers capable of production at a substantially equivalent cost, our clinical trials may be delayed or we could lose potential revenue.

Finally, legislative proposals are pending that, if enacted, could negatively impact U.S. funding for certain biotechnology providers, including some of our vendors, that may have relationships with certain foreign governments or are viewed as posing a threat to national security. This could result in our inability to continue to engage with one or more of our vendors or impair our ability

to contract with new vendors, which could result in supply delays or shortages, clinical trial delays and the need to engage new vendors in a competitive marketplace.

Our current and anticipated future dependence upon third parties for the manufacture of any product candidates we develop may adversely affect our development programs and our ability to commercialize any products that receive marketing approval on a timely and competitive basis.

We may from time to time be dependent on single-source suppliers for some of the components and materials used in our product candidates.

Although we currently do not use any single-source supplier, we may from time to time depend on such suppliers for some of the components and materials used in our product candidates. We cannot ensure that these suppliers or service providers will remain in business, have sufficient capacity or supply to meet our needs or that they will not be purchased by one of our competitors or another company that is not interested in continuing to work with us. Our use of single-source suppliers of raw materials, components, key processes and finished goods could expose us to several risks, including disruptions in supply, price increases or late deliveries. There are, in general, relatively few alternative sources of supply for substitute components. These vendors may be unable or unwilling to meet our future demands for our clinical trials or commercial sale. Establishing additional or replacement suppliers for these components, materials and processes could take a substantial amount of time and it may be difficult to establish replacement suppliers who meet regulatory requirements. Any disruption in supply from any single-source supplier or service provider could lead to supply delays or interruptions which would damage our business, financial condition, results of operations and prospects.

If we are required to switch to a replacement supplier, the manufacture and delivery of our product candidates could be interrupted for an extended period, which could adversely affect our business. Establishing additional or replacement suppliers, if required, may not be accomplished quickly. If we are able to find a replacement supplier, the replacement supplier would need to be qualified and may require additional regulatory authority approval, which could result in further delay. In the event that we should depend on single-source suppliers, we would seek to maintain adequate inventory of the single source components and materials used in our products; however, any interruption or delay in the supply of components or materials, or our inability to obtain components or materials from alternate sources at acceptable prices in a timely manner, could impair our ability to meet the demand for our investigational medicines.

We may enter into collaborations with third parties for the research, development and commercialization of certain of our product candidates. If any such collaborations are not successful, we may not be able to capitalize on the market potential of those product candidates.

We may seek third-party collaborators for the research, development and commercialization of certain of our product candidates. If we enter into any such arrangements with any third parties, we will likely have limited control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of any product candidates we may seek to develop with them. 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. We cannot predict the success of any collaboration that we enter into.

Collaborations involving our research programs or our product candidates pose numerous risks to us, including the following:

- collaborators would have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborators may not pursue development and commercialization of our product candidates or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborator's strategic focus or available funding or external factors such as an acquisition that diverts resources or creates competing priorities;
- collaborators may delay programs, preclinical studies or clinical trials, provide insufficient funding for programs, preclinical studies or clinical trials, stop a preclinical study or clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- collaborators may be acquired by a third party having competitive products or different priorities, causing the emphasis on our product development or commercialization program under such collaboration to be delayed, diminished or terminated;
- collaborators with marketing and distribution rights to one or more products may not commit sufficient resources to the marketing and distribution of such product or products;

- 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 as to invite litigation that could jeopardize or invalidate our proprietary information or expose us to potential litigation;
- disputes may arise between the collaborators and us that result in the delay or termination of the research, development, or commercialization of our product candidates or that result in costly litigation or arbitration that diverts management attention and resources;
- we may lose certain valuable rights under certain circumstances, including if we undergo a change of control;
- collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the affected product candidates; and
- collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all.

If our collaborations do not result in the successful development and commercialization of product candidates, or if one of our collaborators terminates its agreement with us, we may not receive any future research 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 could be delayed, and we may need additional resources to develop product candidates. In addition, if one of our collaborators terminates its agreement with us, we may find it more difficult to find a suitable replacement collaborator or attract new collaborators, and our development programs may be delayed or the perception of us in the business and financial communities could be adversely affected. All of the risks relating to product development, regulatory approval and commercialization described in this 10-K apply to the activities of our collaborators.

These relationships, or those like them, may require us to incur non-recurring and other charges, increase our near- and long-term expenditures, issue securities that dilute our existing stockholders, or disrupt our management and business. In addition, we could face significant competition in seeking appropriate collaborators, and the negotiation process is time-consuming and complex. Our ability to reach a definitive collaboration agreement 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 several factors. If we license rights to any product candidates we or our collaborators may develop, we may not be able to realize the benefit of such transactions if we are unable to successfully integrate them with our existing operations and company culture.

If conflicts arise between us and our potential collaborators, these parties may act in a manner adverse to us and could limit our ability to implement our strategies.

If conflicts arise between us and our potential collaborators, the other party may act in a manner adverse to us and could limit our ability to implement our strategies. Our collaborators may develop, either alone or with others, products in related fields that are competitive with our product candidates that are the subject of these collaborations with us. Competing products, either developed by the collaborators or to which the collaborators have rights, may result in the withdrawal of support for our product candidates. Some of our future collaborators could also become our competitors. Our collaborators could develop competing products, preclude us from entering into collaborations with their competitors, fail to obtain timely regulatory approvals, terminate their agreements with us prematurely, fail to devote sufficient resources to the development and commercialization of products, or merge with or be acquired by a third party who may do any of these things. Any of these developments could harm our product development efforts.

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

Our product development and research programs and the potential commercialization of our product candidates will require substantial additional cash to fund expenses. For some of our product candidates, we may decide to collaborate with other pharmaceutical and biotechnology companies for the development and potential commercialization of those product candidates.

We face significant competition in seeking appropriate 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 the design or results of clinical trials, the likelihood of approval by the FDA, the EMA or comparable foreign regulatory authorities, 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, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge, and industry and market conditions generally. The collaborator 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.

Collaborations are complex and time-consuming to negotiate and document. 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.

We may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of the product candidate for which we are seeking to collaborate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization, reduce the scope of any sales or marketing activities, or increase our own expenditures on the development of the product candidate.

We are dependent on third-party vendors to provide certain licenses, products and services and our business and operations, including clinical trials, could be disrupted by any problems with our significant third-party vendors.

We engage a number of third-party suppliers and service providers to supply critical goods and services, such as contract research services, contract manufacturing services and information technology services. Disruptions to the business, financial stability or operations of these suppliers and service providers, including due to strikes, labor disputes or other disruptions to the workforce, for instance, if, as a result of a pandemic or health epidemic, employees are not able to come to work, or to their willingness and ability to produce or deliver such products or provide such services in a manner that satisfies the requirements put forth by the authorities, or in a manner that satisfies our own requirements, could affect our ability to develop and market our future product candidates on a timely basis. If these suppliers and service providers were unable or unwilling to continue to provide their products or services in the manner expected, or at all, we could encounter difficulty finding alternative suppliers. Even if we are able to secure appropriate alternative suppliers in a timely manner, costs for such products or services could increase significantly. Any of these events could adversely affect our results of operations and our business.

Risks Related to Regulatory Approval and Other Regulatory and Legal Compliance Matters

Our lead product candidates are in clinical development, while all of our other product candidates are still in preclinical development. As an organization, we have only completed one clinical trial and initiated one other Phase 1 clinical trial and three Phase 2 clinical trials and may be unable to do so for any of our other product candidates nor carry out or complete further studies for our lead candidate.

Although we are currently in clinical development for two product candidates, we have no experience as a company in conducting, completing and managing the full suite of clinical trials necessary to obtain regulatory approvals, including approval by the FDA, the EMA or comparable foreign regulatory authorities, or in obtaining approval of any of our product candidates. We are early in our development efforts for our product candidates, and we have successfully completed a Phase 1 clinical trial and initiated Phase 2 trials for our lead product candidate, PGN-EDO51, except in the U.S. where the FDA issued a clinical hold on the initiation of our planned CONNECT2 clinical trial, and initiated an additional Phase 1 and a Phase 2 clinical trial for our second product candidate, PGN-EDODM1. We will need to successfully complete IND- or CTA-enabling activities, early-stage, later-stage and pivotal clinical trials, in order to obtain FDA, EMA or comparable foreign regulatory approval to market PGN-EDO51, PGN-EDODM1, and any future product candidates.

Carrying out clinical trials and the submission of a successful NDA is a complicated process. We completed our first Phase 1 clinical trial for PGN-EDO51 in the third quarter of 2022, and we began dosing participants in CONNECT1 in Canada in January 2024. We received clearance from the MHRA in February 2024 to initiate CONNECT2 in the U.K. in boys and young men living with DMD.

Based on the observed high tissue concentrations of oligonucleotide and exon skipping in muscle in our Phase 1 trial of PGN-EDO51 in HVs, as well as the early data from the low dose (5 mg/kg) cohort in our CONNECT1 Phase 2 trial of PGN-EDO51, we believe that these results could signal the potential for the accumulation of exon 51 skipped transcript and higher production of dystrophin protein in muscle tissue with repeated doses of PGN-EDO51 in DMD patients over a longer treatment period. However, our belief based on this data may be erroneous and, to date, the FDA has not allowed the initiation of the planned CONNECT2 clinical trial in the U.S., placing that trial on clinical hold. Moreover, we have received communication from Health Canada that dosing of participants in the 5 and 10 mg/kg cohorts in our CONNECT1 Phase 2 study may continue at their current dose levels. Health Canada has requested additional information from us to address its safety concerns before any further dose escalation or enrollment of any additional participants at the current dose levels in the CONNECT1 study. It is unknown whether Health Canada will allow us to further dose escalate or enroll additional participants in this study. There can be no assurance that our expectations of higher exon skipping and dystrophin production will be reflected in continued Phase 2 clinical evaluation of PGN-EDO51 in DMD patients.

In addition, based on our observations in preclinical studies that treatment with PGN-EDODM1 led to robust correction of mis-splicing and myotonia, as well as the robust dose-dependent splicing correction observed in the initial data from the 5 and 10 mg/kg cohorts in our FREEDOM Phase 1 study, we believe PGN-EDODM1 has the potential to lead to meaningful functional improvements with repeat dosing over time. However, our belief based on this data may be erroneous. There can be no assurance that our

expectations of robust splicing correction and improved functional outcomes will be reflected in continued clinical evaluation of PGN-EDODM1 in DM1 patients, including in our ongoing FREEDOM2 MAD study.

Although we completed a Phase 1 clinical trial for our lead product candidate and have several additional clinical trials ongoing, we have not completed any additional clinical trials, and have limited experience as a company in preparing, submitting and prosecuting regulatory filings. In addition, we have had limited interactions with the FDA, the EMA and comparable foreign regulatory authorities and cannot be certain how many clinical trials of PGN-EDO51, PGN-EDODM1, or any other product candidates will be required or how such trials should be designed. For example, the FDA has approved at least four drugs based on their minimal dystrophin production, and it is our belief that we may be able to pursue an accelerated approval pathway for PGN-EDO51 on that same basis, assuming we continue to see increases in exon skipping and dystrophin production with higher doses and a longer treatment period. The FDA has previously provided feedback on our clinical trials for PGN-EDO51, as well as for PGN-EDODM1, and we have addressed their feedback in our clinical trial designs. To date, we have not received FDA feedback on any potential accelerated approval pathway for PGN-EDO51 and currently a clinical hold is in place for the initiation of CONNECT2 in the U.S. We may be unable to successfully resolve our current clinical hold and efficiently execute and complete necessary clinical trials for our product candidates in a way that leads to regulatory submission and approval of any of our product candidates, including potentially any accelerated approval. We may require more time and incur greater costs than our competitors and may not succeed in obtaining regulatory approvals of product candidates that we develop. Failure to commence or complete, or delays in, our current or planned clinical trials, could prevent us from or delay us in submitting NDAs for and commercializing our product candidates.

Even if we complete the necessary preclinical studies and clinical trials, the marketing approval process is expensive, time-consuming and uncertain and may prevent us from obtaining approvals for the commercialization of our product candidates. If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals, we will not be able to commercialize, or will be delayed in commercializing, our product candidates, and our ability to generate revenue will be materially impaired.

Our product candidates and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale and distribution, are subject to comprehensive regulation by the FDA and other regulatory authorities in the U.S., the EMA and comparable authorities in other countries. Failure to obtain marketing approval for a product candidate will prevent us from commercializing the product candidate in a given jurisdiction. We have not received approval to market any product candidates from regulatory authorities in any jurisdiction.

We have no experience as a company in submitting and supporting the applications necessary to gain marketing approvals and may need to rely on third parties to assist us in this process. Securing regulatory approval requires the submission of extensive preclinical and clinical data and supporting information to the various regulatory authorities for each therapeutic indication to establish the product candidate's safety and effectiveness. Securing regulatory approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the relevant regulatory authority. Our product candidates may not be effective, may be only moderately effective or may prove to have undesirable or unintended side effects, toxicities, or other characteristics that may preclude our obtaining marketing approval or prevent or limit commercial use.

The process of obtaining marketing approvals, both in the U.S. and abroad, is expensive, may take many years if additional clinical trials are required, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. Of the large number of products in development, only a small percentage successfully complete the FDA, EMA or foreign regulatory approval processes and are commercialized. Even if our product candidates demonstrate safety and efficacy in clinical trials, the regulatory agencies may not complete their review processes in a timely manner, or we may not be able to obtain regulatory approval. Additional delays may result if an FDA Advisory Committee or other regulatory authority recommends non-approval or restrictions on approval. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application. The FDA, the EMA and comparable foreign regulatory authorities in other countries have substantial discretion in the approval process and may refuse to accept any application or may decide that our data is insufficient for approval and require additional preclinical, clinical or other studies. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent marketing approval of a product candidate. Moreover, the U.S. Supreme Court's July 2024 decision to overturn prior established case law giving deference to regulatory agencies' interpretations of ambiguous statutory language has introduced uncertainty regarding the extent to which FDA's regulations, policies, and decisions may become subject to increasing legal challenges, delays, and/or changes. If we experience delays in obtaining approval or if we fail to obtain approval of our product candidates, the commercial prospects for those product candidates may be harmed, and our ability to generate revenues will be materially impaired.

The FDA also has substantial discretion in the approval process. The number and types of preclinical studies and clinical trials that will be required for NDA approval varies depending on the product candidate, the disease or the condition that the product candidate is designed to treat and the regulations applicable to any particular product candidate. Despite the time and expense associated with preclinical studies and clinical trials, failure can occur at any stage.

Clinical trial failure may result from a multitude of factors including flaws in trial design, dose selection, patient enrollment criteria and failure to demonstrate favorable safety or efficacy traits, and failure in clinical trials can occur at any stage. Companies in the drug development industry frequently suffer setbacks in the advancement of clinical trials due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier trials. Based upon negative or inconclusive results, we may decide, or regulators may require us, to conduct additional clinical trials or preclinical studies. In addition, data obtained from clinical trials is susceptible to varying interpretations, and regulators may not interpret our data as favorably as we do, which may further delay, limit or prevent marketing approval.

The FDA or any foreign regulatory authority could delay, limit or deny approval of a product candidate for many reasons, including because the FDA or such other regulatory authority:

- may disagree with the design or implementation of our trials;
- may not deem a product candidate to be safe or effective for its intended uses;
- determines that the product candidate does not have an acceptable benefit-risk profile;
- may not agree that the data collected from preclinical studies and clinical trials are acceptable or sufficient to support the submission of an NDA or other submission or to obtain regulatory approval, and may impose requirements for additional preclinical studies or clinical trials;
- may determine that adverse events experienced by participants in our clinical trials represent an unacceptable level of risk;
- may determine that the population studied in the clinical trial may not be sufficiently broad or representative to assure safety in the full population for which we seek approval;
- may not accept clinical data from trials that are conducted at clinical facilities or in countries where the standard of care is potentially different from that of the U.S.;
- may disagree regarding the formulation, labeling and/or specifications;
- may not approve the manufacturing processes associated with a product candidate or may determine that a manufacturing facility does not have an acceptable compliance status;
- may change approval policies or adopt new regulations; or
- may not file a submission due to, among other reasons, the content or formatting of the submission.

Even if we eventually complete clinical testing and receive approval of an NDA or foreign marketing application for any product candidates, the FDA, EMA or applicable foreign regulatory authority may grant approval or other marketing authorization contingent on the performance of costly additional clinical trials, including post-market clinical trials. For example, we expect that the FDA will require a confirmatory trial of PGN-EDO51, if it is approved under the accelerated approval regulations. The FDA, EMA or the applicable foreign regulatory authority also may approve or authorize for marketing a product candidate for a more limited indication or patient population that we originally request, and the FDA, EMA or applicable foreign regulatory authority may not approve or authorize the labeling that we believe is necessary or desirable for the successful commercialization of a product candidate. Any of these restrictions or commitments could render an approved product not commercially viable, which would materially adversely impact our business and prospects.

Obtaining and maintaining marketing approval or commercialization of our product candidates in the U.S. does not mean that we will be successful in obtaining marketing approval of our product candidates in other jurisdictions. Failure to obtain marketing approval in foreign jurisdictions would prevent our product candidates from being marketed in such jurisdictions, which, in turn, would materially impair our ability to generate revenue.

In order to market and sell our product candidates in the EU and many other foreign jurisdictions, we or our collaborators must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The regulatory approval process outside the U.S. generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the U.S., it is required that the product be approved for reimbursement before the product can be approved for sale in that country. We or these third parties may not obtain approvals from regulatory authorities outside the U.S. on a timely basis, if at all. Approval by the FDA does not ensure approval by the EMA or regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the U.S. does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. Furthermore, now that the U.K. is no longer part of the EU, a separate authorization is needed to market medicinal products in the U.K. We may not be able to file for marketing approvals and may not receive the necessary approvals to commercialize our medicines in any jurisdiction, which would materially impair our ability to generate revenue.

Any delay in obtaining, or an inability to obtain, any marketing approvals would prevent us from commercializing any product candidates in the U.K. and/or the EU and/or other foreign jurisdictions and restrict our ability to generate revenue and achieve and sustain profitability. If any of these outcomes occur, we may be forced to restrict or delay efforts to seek regulatory approval in the U.K. and/or the EU and/or other foreign jurisdictions for our product candidates, which could significantly and materially harm our business.

We may attempt to seek approval from the FDA or comparable foreign regulatory authorities, where applicable, under the accelerated approval pathways. We may fail to obtain approval under such accelerated approval pathways. Moreover, these pathways may not lead to a faster development, regulatory review or approval process and do not increase the likelihood that our product candidates will receive marketing approval.

We may in the future seek accelerated approval, where applicable, under the FDA's accelerated approval pathway. A product may be eligible for accelerated approval if it treats a serious or life-threatening condition, generally provides a meaningful advantage over available therapies, and demonstrates an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit or on a clinical endpoint that can be measured earlier than IMM, that is reasonably likely to predict an effect on IMM or other clinical benefit. As a condition of accelerated approval, the FDA likely would require that we perform adequate and well-controlled post-marketing clinical trials to confirm the product's clinical benefit. These confirmatory trials must be completed with due diligence. Under FDORA, the FDA is permitted to require, as appropriate, that a post-approval confirmatory study or studies be underway prior to approval or within a specified time period after the date of accelerated approval was granted. FDORA also requires sponsors to send updates to the FDA every 180 days on the status of such studies, including progress toward enrollment targets, and the FDA must promptly post this information publicly. FDORA also gives the FDA increased authority to withdraw approval of a drug or biologic granted accelerated approval on an expedited basis if the sponsor fails to conduct such studies in a timely manner, send the necessary updates to the FDA, or if such post-approval studies fail to verify the drug's predicted clinical benefit. Under FDORA, the FDA is empowered to take action, such as issuing fines, against companies that fail to conduct with due diligence any post-approval confirmatory study or submit timely reports to the agency on their progress. We have reported encouraging early results from the first cohort in our Phase 2 CONNECT1 study of PGN-EDO51 and believe that with a longer treatment period and higher doses of PGN-EDO51, we may see higher levels of exon skipped transcript potentially resulting in significant increases in dystrophin. If we continue to receive positive results from our CONNECT1 study and receive positive results from the CONNECT2 study for PGN-EDO51 that show an acceptable safety and tolerability profile; a clinically meaningful increase in dystrophin levels, a surrogate endpoint, in the biceps of DMD patients; and robust exon skipping levels in the same tissue; we intend to pursue this accelerated approval pathway subject to discussions with the FDA. However, we have received communication from Health Canada that dosing of participants in the 5 and 10 mg/kg cohorts may continue at their current dose levels, but currently Health Canada will not allow us to dose escalate or enroll additional participants in our CONNECT1 Phase 2 trial and the initiation of our CONNECT2 Phase 2 trial is on clinical hold in the U.S. Even if we obtain clearance from Health Canada to further dose escalate and enroll more participants in the CONNECT1 trial and we obtain clearance from the FDA to initiate our CONNECT2 Phase 2 trial in the U.S., these Phase 2 trials may fail to produce such supportive clinical data, and we may be unable to pursue the accelerated approval pathway as planned. To date we have not received FDA feedback on any potential accelerated approval pathway for PGN-EDO51.

In addition, the FDA currently requires, unless otherwise informed by the agency, pre-approval of promotional materials for products receiving accelerated approval, which could adversely impact the timing of the commercial launch of the product. Thus, even if we seek to utilize the accelerated approval pathway, we may not be able to obtain accelerated approval and, even if we do, we may not experience a faster development, regulatory review or approval process for that product. In addition, receiving accelerated approval does not assure that the product's accelerated approval will eventually be converted to a full approval.

In the EU, under the centralized procedure, the EMA's CHMP may perform an accelerated assessment of a marketing authorization application. Applicants requesting an accelerated assessment procedure must justify that the product candidate is expected to be of major public health interest, particularly from the point of view of therapeutic innovation. Prior to seeking accelerated approval for any of our product candidates, we intend to seek feedback from the FDA or similar foreign regulatory authorities and will otherwise evaluate our ability to seek and receive accelerated approval. There can be no assurance that after our evaluation of the feedback and other factors we will decide to pursue or submit an NDA or similar application for accelerated approval or any other form of expedited development or review. Similarly, there can be no assurance that after subsequent FDA or similar foreign regulatory authorities feedback we will continue to pursue or apply for accelerated approval or any other form of expedited development or review, even if we initially decide to do so. Furthermore, if we decide to submit an application for accelerated approval or other expedited development or review for our product candidates, there can be no assurance that such submission or application will be accepted or that any expedited development or review will be granted on a timely basis, or at all. The FDA or other comparable foreign regulatory authorities could also require us to conduct further studies prior to considering our application or granting approval of any type. A failure to obtain accelerated approval or any other form of expedited development or review for our product candidate would result in a longer time period to commercialization of such product candidate, if any, could increase the cost of development of such product candidate, and could harm our competitive position in the marketplace.

We may seek one or more designations or expedited programs for one or more of our product candidates, but we might not receive such designations or be allowed to proceed on expedited program pathways, and even if we do and proceed on such expedited program pathways in the future, such designations or expedited programs may not lead to a faster development or regulatory review or approval process, and each designation does not increase the likelihood that any of our product candidates will receive marketing approval in the U.S.

We have received fast-track designation for PGN-EDODM1 for the treatment of DM1 and may seek fast-track designation for some of our other product candidates. If a drug is intended for the treatment of a serious or life-threatening condition and nonclinical or clinical data for the drug demonstrates the potential to address an unmet medical need for such a condition, the drug sponsor may apply for fast-track designation. The FDA has broad discretion whether or not to grant this designation, so even if we believe a particular product candidate is eligible for this designation, we cannot assure you that the FDA would decide to grant it for any of our other product candidates. Even with fast-track designation, we may not experience a faster development process, review or approval compared to conventional FDA procedures. The FDA may withdraw fast-track designation if it believes that the designation is no longer supported by data from our clinical development program. Fast-track designation alone does not guarantee qualification for the FDA's priority review procedures.

We may seek a breakthrough therapy designation for some of our product candidates. A breakthrough therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For drugs that have been designated as breakthrough therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens. Drugs designated as breakthrough therapies by the FDA may also be eligible for priority review and accelerated approval. Designation as a breakthrough therapy is within the discretion of the FDA. Accordingly, even if we believe one of our product candidates meets the criteria for designation as a breakthrough therapy, the FDA may disagree and instead determine not to make such designation. In any event, the receipt of a breakthrough therapy designation for a product candidate may not result in a faster development process, review or approval compared to therapies considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our product candidates qualify as breakthrough therapies, the FDA may later decide that such product candidates no longer meet the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

If the FDA determines that a product candidate offers a treatment for a serious condition and, if approved, the product would provide a significant improvement in safety or effectiveness, the FDA may designate the product candidate for priority review. A priority review designation means that the goal for the FDA to review and take action on an application is six months, rather than the standard review period of ten months. We may request priority review for our product candidates. The FDA has broad discretion with respect to whether or not to grant priority review status to a product candidate, so even if we believe a particular product candidate is eligible for such designation or status, the FDA may decide not to grant it. Moreover, a priority review designation does not necessarily result in an expedited regulatory review or approval process or necessarily confer any advantage with respect to approval compared to conventional FDA procedures. Receiving priority review from the FDA does not guarantee approval within the six-month review cycle or at all.

We may pursue orphan drug designation for certain of our product candidates, and we may not be able to obtain such designation, or obtain or maintain the benefits of such designation including orphan drug exclusivity, and even if we do, that exclusivity may not prevent regulatory authorities from approving other competing products.

In September 2023, the FDA granted orphan drug designation to PGN-EDODM1 for the treatment of DM1 and in March 2024, the FDA granted orphan drug designation to PGN-EDO51 for the treatment of DMD patients whose mutations are amenable to an exon 51-skipping approach. We intend to seek orphan drug designation for some of our other product candidates; however, we may never receive such designations. Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is a drug or biologic intended to treat a rare disease or condition, defined as a patient population of fewer than 200,000 in the U.S., or a patient population greater than 200,000 in the U.S. where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the U.S. Orphan drug designation must be requested before submitting an NDA. A similar regulatory scheme governs orphan products in the EU.

Orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and application 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. In addition, if a product candidate with an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the product is entitled to a period of marketing exclusivity, which precludes the FDA from approving another marketing application for the same product for the same therapeutic indication for seven years.

Even if we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different products can be approved for the same condition. In addition, even after an orphan drug is approved, the FDA can subsequently approve the same product for the same condition if the FDA concludes that the later product is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care. Orphan drug exclusivity may also be lost if the FDA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the product to meet the needs of the patients with the rare disease or condition. Further, even if we obtain orphan drug designation, we may not be the first to obtain marketing approval for any particular orphan indication due to the uncertainties associated with developing pharmaceutical products.

The FDA may further reevaluate the Orphan Drug Act and its regulations and policies. We do not know if, when, or how the FDA may change the orphan drug regulations and policies in the future, and it is uncertain how any changes might affect our business. Depending on what changes the FDA may make to its orphan drug regulations and policies, our business could be adversely impacted.

A marketing application for a product candidate with RPDD, if approved, may not meet the eligibility criteria for a Priority Review Voucher, or PRV, or the RPDD program may sunset before the FDA is able to consider eligibility for a voucher.

Designation of a drug as a product for a rare pediatric disease does not guarantee that a marketing application for such drug will meet the eligibility criteria for a rare pediatric disease PRV at the time the application is approved. While we have received RPDD from the FDA for PGN-EDO51 for the treatment of DMD patients who are amenable to exon 51 skipping, we would need to request a rare pediatric disease PRV in the marketing application of PGN-EDO51. The FDA may determine that any such marketing application, if approved, does not meet the eligibility criteria for a PRV. The FDA's rare pediatric disease priority review voucher program began to sunset on December 20, 2024 on failure to pass a continuing resolution package that included its reauthorization. Under the amended statutory provisions, after December 20, 2024, the FDA may award rare pediatric disease PRVs for an approved rare pediatric disease product application only if the sponsor has rare pediatric disease designation for the drug and if that designation was granted by December 20, 2024. After September 30, 2026, the FDA may not award any rare pediatric disease priority review vouchers. We understand that the FDA continues to review designation requests despite this program beginning to sunset. Congress may vote to reauthorize this program, but its future remains unknown at this time. If a marketing application for PGN-EDO51 is not approved prior to September 30, 2026 for any reason, regardless of whether it meets the criteria for a rare pediatric disease PRV, it will not be eligible for a PRV, unless the authority for FDA to award rare pediatric disease PRVs is further extended through federal lawmaking.

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

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

Even if we receive regulatory approval for any of our product candidates, we will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense. Additionally, our product candidates, if approved, could be subject to post-market study requirements, marketing and labeling restrictions, and even recall or market withdrawal if unanticipated safety issues are discovered following approval. In addition, we may be subject to penalties or other enforcement action if we fail to comply with regulatory requirements.

The FDA, the EMA or a comparable foreign regulatory authority may not approve any of our product candidates derived from our platform. However, if the FDA, EMA or comparable foreign regulatory authority approves any of our product candidates, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion and recordkeeping

for the product will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, conformance with applicable product tracking and tracing requirements, establishment registration and listing, as well as continued compliance with cGMPs and GCPs for any clinical trials that we conduct post-approval. Any regulatory approvals that we receive for our product candidates may also be subject to limitations on the approved indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing studies, and surveillance to monitor the safety and efficacy of the product. Additionally, under FDORA, sponsors of approved drugs and biologics must provide six months' notice to the FDA of any changes in marketing status, such as the withdrawal of a drug, and failure to do so could result in the FDA placing the product on a list of discontinued products, which would revoke the product's ability to be marketed. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things:

- restrictions on the marketing or manufacturing of the product, withdrawal of the product from the market, or voluntary or mandatory product recalls;
- restrictions on our ability to conduct clinical trials, including full or partial clinical holds on ongoing or planned trials;
- restrictions on product distribution or use, or requirements to conduct post-marketing studies or clinical trials;
- fines, warning letters or other regulatory enforcement action;
- refusal by the FDA, the EMA or comparable foreign regulatory authorities to approve pending applications or supplements to approved applications filed by us;
- product seizure or detention, or refusal to permit the import or export of products; and
- injunctions or the imposition of civil or criminal penalties.

The occurrence of any event or penalty described above may inhibit our ability to commercialize our product candidates and generate revenue and could require us to expend significant time and resources in response and could generate negative publicity. In addition, the FDA's, EMA's and other foreign regulatory authorities' policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval 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, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained, which would adversely affect our business, prospects and ability to achieve or sustain profitability.

Any product candidate for which we obtain marketing approval will be subject to restrictions, such as the laws and regulations prohibiting the promotion of off-label uses, or may need to be withdrawn from the market, and we may be subject to substantial penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our medicines, when and if any of them are approved.

The FDA, EMA and other foreign regulatory authorities closely regulate the post-approval marketing and promotion of medicines to ensure that they are marketed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA, EMA and other foreign regulatory authorities impose stringent restrictions on manufacturers' communications regarding off-label use. In particular, a product may not be promoted for uses that are not approved by the FDA, EMA and other foreign regulatory authorities as reflected in the product's approved labeling. If we receive marketing approval for a product candidate, physicians may nevertheless prescribe it to their patients in a manner that is inconsistent with the approved label. If we are found to have promoted such off-label uses, we may be subject to enforcement action for off-label marketing by the FDA and other federal and state enforcement agencies, including the Department of Justice. Violation of the FDCA and other statutes, including the False Claims Act, relating to the promotion and advertising of prescription products may also lead to investigations or allegations of violations of federal and state healthcare fraud and abuse laws and state consumer protection laws. The federal government has levied large civil and criminal fines against companies for alleged improper promotion of off-label use and has enjoined several companies from engaging in off-label promotion. The government has also required companies to enter into consent decrees and/or imposed permanent injunctions under which specified promotional conduct is changed or curtailed. If we cannot successfully manage the promotion of our product candidates, if approved, we could become subject to significant liability, which would materially adversely affect our business and financial condition.

In addition, later discovery of previously unknown problems with our medicines, manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may yield various results, including:

- restrictions on such medicines, manufacturers or manufacturing processes;
- restrictions on the labeling or marketing of a medicine;

- restrictions on the distribution or use of a medicine;
- requirements to conduct post-marketing clinical trials;
- receipt of warning or untitled letters;
- withdrawal of the medicines from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of medicines;
- fines, restitution or disgorgement of profits or revenue;
- suspension or withdrawal of marketing approvals;
- suspension of any ongoing clinical trials;
- refusal to permit the import or export of our medicines;
- product seizure; and
- injunctions or the imposition of civil or criminal penalties.

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 ability to commercialize any product candidates we develop and adversely affect our business, financial condition, results of operations and prospects.

Additionally, if any of our product candidates receive marketing approval, the FDA could require us to adopt a REMS to ensure that the benefits outweigh its risks, which may include, among other things, a medication guide outlining the risks of the product for distribution to patients and a communication plan to healthcare practitioners. Furthermore, if we or others later identify undesirable side effects caused by our product candidate, several potentially significant negative consequences could result, including:

- regulatory authorities may suspend or withdraw approvals of such product candidate;
- regulatory authorities may require additional warnings on the label;
- we may be required to change the way a product candidate is administered or conduct additional clinical trials;
- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

We and our contract manufacturers are subject to significant regulation. The manufacturing facilities on which we rely may not continue to meet regulatory requirements, which could materially harm our business.

All entities involved in the preparation of product candidates for clinical trials or commercial sale, including any contract manufacturers, are subject to extensive regulation. Components of a finished therapeutic product approved for commercial sale or used in late-stage clinical trials must be manufactured in accordance with cGMP regulations. These regulations govern manufacturing processes and procedures (including record keeping) and the implementation and operation of quality systems to control and assure the quality of investigational products and products approved for sale. Poor control of production processes can lead to the introduction of adventitious agents or other contaminants or to inadvertent changes in the properties or stability of our product candidates that may not be detectable in final product testing. We or our contract manufacturers must supply all necessary documentation in support of an NDA on a timely basis and must adhere to the FDA's cGMP regulations enforced through its facilities inspection program. Our facilities and quality systems and the facilities and quality systems of some or all of our third-party contractors must pass a pre-approval inspection for compliance with the applicable regulations as a condition of regulatory approval of our product candidates. In addition, the regulatory authorities may, at any time, audit or inspect a manufacturing facility involved with the preparation of our product candidates or our other potential products or the associated quality systems for compliance with the regulations applicable to the activities being conducted. If these facilities do not pass a pre-approval plant inspection, FDA approval of the products will not be granted.

The regulatory authorities also may, at any time following approval of a product for sale, audit any of our future manufacturing facilities or those of our third-party contractors. If any such inspection or audit identifies a failure to comply with applicable regulations or if a violation of our product specifications or applicable regulations occurs independent of such an inspection or audit, we or the relevant regulatory authority may require remedial measures that may be costly and/or time-consuming for us or a third party to implement and that may include the temporary or permanent suspension of a clinical trial or commercial sales or the

temporary or permanent closure of a facility. Any such remedial measures imposed upon us or third parties with whom we contract could materially harm our business.

If we or any of our third-party manufacturers fail to maintain regulatory compliance, the FDA can impose regulatory sanctions including, among other things, refusal to approve a pending application for a new product, or revocation of a pre-existing approval. Any such consequence would severely harm our business, financial condition and results of operations.

If we or any contract manufacturers and suppliers we engage 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 contract manufacturers and suppliers we engage 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. 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 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 hazardous waste insurance coverage, and our property, casualty and general liability insurance policies specifically exclude coverage for damages and fines arising from 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 could be suspended.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws, regulations and permitting 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 also may result in substantial fines, penalties or other sanctions or business disruption. Any third-party contract manufacturers and suppliers we engage will also be subject to these and other environmental, health and safety laws and regulations. Liabilities they incur pursuant to these laws and regulations could result in significant costs or an interruption in operations, which could in turn have a material adverse effect on our business, financial condition, results of operations and prospects.

Shutdowns or 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.

Currently, federal agencies in the U.S. are operating under a continuing resolution that is set to expire on March 14, 2025. Without appropriation of additional funding to federal agencies, our business operations related to our product development activities for the U.S. market could be impacted. The ability of the FDA 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 ability to hire and retain key personnel and accept the payment of user fees, and other events that may otherwise affect the FDA's ability to perform routine functions. Average review times at the FDA 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 may also slow the time necessary for new drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, including for 35 days beginning on December 22, 2018, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical FDA employees and stop critical activities.

During the COVID-19 public health emergency, a number of companies announced receipt of complete response letters due to the FDA's inability to complete required inspections for their applications. 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.

Our relationships with healthcare providers, physicians and third-party payors will be subject to applicable anti-kickback, fraud and abuse, and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.

Healthcare providers, physicians and third-party payors play a primary role in the recommendation and prescription of any product candidates that we develop for which we obtain marketing approval. Our future arrangements with third-party payors and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we research, market, sell and distribute our medicines for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations include, without limitation, the federal Anti-Kickback Statute, the federal civil and criminal False Claims Act and Physician Payments Sunshine Act and regulations. For more information, see “*Business – Healthcare Regulation – Other Healthcare Laws*” in this 10-K.

Additionally, we are subject to state and foreign equivalents of each of these healthcare laws and regulations, among others, some of which may be broader in scope and may apply regardless of the payor. Many U.S. states have adopted laws similar to the federal Anti-Kickback Statute and False Claims Act, and may apply to our business practices, including, but not limited to, research, distribution, sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental payors, including private insurers. In addition, some states have passed laws that require pharmaceutical companies to comply with the April 2003 Office of Inspector General Compliance Program Guidance for Pharmaceutical Manufacturers and/or the Pharmaceutical Research and Manufacturers of America’s Code on Interactions with Healthcare Professionals. Several states also impose other marketing restrictions or require pharmaceutical companies to make marketing or price disclosures to the state and require the registration of pharmaceutical sales representatives.

The provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products is prohibited in the EU and U.K. The provision of benefits or advantages to induce or reward improper performance generally is typically governed by the national anti-bribery laws of European Union Member States, and the Bribery Act 2010 in the U.K. Infringement of these laws could result in substantial fines and imprisonment. EU Directive 2001/83/EC, which is the EU Directive governing medicinal products for human use, further provides that, where medicinal products are being promoted to persons qualified to prescribe or supply them, no gifts, pecuniary advantages or benefits in kind may be supplied, offered or promised to such persons unless they are inexpensive and relevant to the practice of medicine or pharmacy. This provision has been transposed into the Human Medicines Regulations 2012 and so remains applicable in the U.K. despite its departure from the EU.

Payments made to physicians in certain EU Member States must be publicly disclosed. Moreover, agreements with physicians often must be the subject of prior notification and approval by the physician’s employer, his or her competent professional organization and/or the regulatory authorities of the individual EU Member States. These requirements are provided in the national laws, industry codes or professional codes of conduct applicable in the EU Member States. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

The scope and enforcement of these laws is uncertain and subject to rapid change in the current environment of healthcare reform, especially in light of the lack of applicable precedent and regulations. Federal and state enforcement has led to a number of investigations, prosecutions, convictions and settlements in the healthcare industry. Ensuring that our internal operations and future business arrangements with third parties comply with applicable healthcare laws and regulations will involve substantial costs. We have entered into consulting and scientific advisory board arrangements with physicians and other healthcare providers, including some who could influence the use of our product candidates, if approved. Compensation under some of these arrangements includes the provision of stock or stock options in addition to cash consideration. 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 administrative, civil and criminal penalties, damages, fines, disgorgement, the exclusion from participation in federal and state healthcare programs, reputational harm, and the curtailment or restructuring of our operations, as well as additional reporting obligations and oversight if we become subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with these laws. Further, defending against any such actions can be costly and time consuming, and may require significant financial and personnel resources. Therefore, even if we are successful in defending against any such actions that may be brought against us, our business may be impaired. If any of the physicians or other 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 criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs and individual imprisonment. If any of the above occur, our ability to operate our business and our results of operations could be adversely affected.

Healthcare legislative reform discourse and potential or enacted measures may increase the difficulty and cost for us and any future collaborators to obtain marketing approval of and commercialize our product candidates and affect the prices we, or they, may obtain.

Payors, whether domestic or foreign, or governmental or private, are developing increasingly sophisticated methods of controlling healthcare costs and those methods are not always specifically adapted for new technologies such as gene therapy and therapies addressing rare diseases such as those we are developing. In both the U.S. and certain foreign jurisdictions, there have been a number of legislative and regulatory changes to the health care system that could impact our ability to sell our products profitably. We expect that current laws, as well as other healthcare reform measures that may be adopted in the future, may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies and in additional downward pressure on the price that we, or any collaborators, may receive for any approved products. For more information, see “Business – Healthcare Regulation – Healthcare Reform and Legislative Updates” in this 10-K.

At the state level, individual states are increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product 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 which suppliers will be included in their prescription drug and other healthcare programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

We cannot predict the initiatives that may be adopted in the future. The continuing efforts of the government, insurance companies, managed care organizations and other payors of healthcare services to contain or reduce costs of healthcare and/or impose price controls may adversely affect:

- the demand for our product candidates, if we obtain regulatory approval;
- our ability to set a price that we believe is fair for our products, if licensed;
- our ability to generate revenue and achieve or maintain profitability;
- the level of taxes that we are required to pay; and
- the availability of capital.

We expect that other healthcare reform measures may be adopted in the future, which may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, lower reimbursement, and new payment methodologies. This could lower the price that we receive for our products. Any denial in coverage or reduction in reimbursement from Medicare or other government-funded programs may result in a similar denial or reduction in payments from private payors, which may prevent us from being able to generate sufficient revenue, attain profitability or commercialize our products. It is not clear how other future potential changes to the ACA will change the reimbursement model and market outlook for our current and future product candidates.

Our employees, principal investigators, consultants and commercial partners may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements and insider trading.

We are exposed to the risk of fraud or other misconduct by our employees, consultants and partners, and in our clinical trials, our principal investigators. Misconduct by these parties could include intentional failures to comply with FDA regulations or the regulations applicable in the EU and other jurisdictions, provide accurate information to the FDA, the European Commission and other regulatory authorities, comply with healthcare fraud and abuse laws and regulations in the U.S. 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, self-dealing and other abusive practices. These laws and regulations restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Such misconduct also could involve the improper use of information obtained in the course of clinical trials or interactions with the FDA, the European Commission and other regulatory authorities, which could result in regulatory sanctions and cause serious harm to our reputation. It is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from government investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, financial condition, results of operations and prospects, including the imposition of significant fines or other sanctions.

Laws and regulations governing any international operations we may have in the future may preclude us from developing, manufacturing and selling certain product candidates outside of the U.S. and require us to develop and implement costly compliance programs.

We are subject to numerous laws and regulations in each jurisdiction outside the U.S. in which we operate. The creation, implementation and maintenance of international business practices compliance programs is costly and such programs are difficult to enforce, particularly where reliance on third parties is required.

The Foreign Corrupt Practices Act, or FCPA, prohibits any U.S. individual or business from paying, offering, or authorizing the provision of money or anything of value, directly or indirectly through parties, to any foreign official, official of a public international organization, or political party official or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the U.S. to comply with certain accounting provisions requiring the company to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations. The anti-bribery provisions of the FCPA are enforced primarily by the Department of Justice. The SEC is involved with enforcement of the books and records provisions of the FCPA.

Compliance with the FCPA and other anti-corruption laws potentially applicable to our business is expensive and difficult, particularly in countries in which corruption is a recognized problem. In addition, compliance with the FCPA and other anti-corruption laws presents particular challenges in the pharmaceutical industry, because, in many countries, hospitals are operated by the government, and doctors and other hospital employees are considered foreign officials.

Various U.S. export and sanctions laws, regulations and executive orders also restrict the use and dissemination outside of the U.S., or the sharing with certain non-U.S. nationals, of certain products and technical data relating to those products. Furthermore, such export and sanctions laws include restrictions or prohibitions on the sale or supply of certain products and services to U.S. embargoed countries or sanctioned countries, governments, persons and entities. Our expansion outside of the U.S. has required, and will continue to require, us to dedicate additional resources to comply with these laws, and these laws may preclude us from developing, manufacturing or selling certain drugs and drug candidates outside of the U.S., which could limit our growth potential and increase our development costs. The failure to comply with laws governing international business practices may result in substantial penalties, including suspension or debarment from government contracting. Violation of the FCPA and export and sanctions laws can result in significant civil and criminal penalties, imprisonment, the loss of export or import privileges, debarment, breach of contract and fraud litigation, reputational harm, and other consequences. Indictment alone under the FCPA can lead to suspension of the right to do business with the U.S. government until the pending claims are resolved. Conviction of a violation of the FCPA can result in long-term disqualification as a government contractor. The termination of a government contract or relationship as a result of our failure to satisfy any of our obligations under laws governing international business practices would have a negative impact on our operations and harm our reputation and ability to procure government contracts. The SEC also may suspend or bar issuers from trading securities on U.S. exchanges for violations of the FCPA's accounting provisions.

We are subject to stringent data protection, privacy, and security laws, regulations, standards and contractual obligations and actual or perceived failure to comply with such requirements could have a material adverse effect on our business, financial condition, results of operations or prospects.

We are subject to data privacy and protection laws, regulations, policies, standards and contractual obligations that impose certain requirements relating to the collection, transmission, storage and use of personal information. The legislative and regulatory landscape for data privacy and protection continues to evolve in jurisdictions worldwide, and there has been an increasing focus on privacy and data protection issues. Actual or perceived failure to comply with laws and regulations governing personal information could result in government investigations and enforcement actions against us, fines, claims for damages by affected third parties, damage to our reputation and loss of goodwill, any of which could have a material adverse effect on our business, financial condition, results of operations or prospects.

The regulatory framework for the collection, use, safeguarding, sharing, transfer and other processing of personal information worldwide is rapidly evolving and is likely to remain uncertain for the foreseeable future. Globally, virtually every jurisdiction in which we operate has established its own data security and privacy frameworks with which we must comply. For example, the collection, use, disclosure, transfer or other processing of personal data, including personal health data, of individuals in the European Economic Area, or EEA, is subject to the EU General Data Protection Regulation, or EU GDPR, as well as national data protection laws in effect in the member states of the EEA, and similar processing of personal data regarding individuals in the U.K. is governed by the U.K. General Data Protection Regulation, or U.K. GDPR and the U.K. Data Protection Act 2018. In this document, "GDPR" refers to both the EU GDPR and the U.K. GDPR, unless specified otherwise. The GDPR imposes stringent requirements on companies that process personal data, including requirements relating to having a legal basis for processing personal data, stricter requirements relating to the processing of sensitive data (such as health data), where required by GDPR - obtaining consent of the individuals to whom the personal data relates, establishing a legal basis for processing, providing information to individuals regarding

data processing activities, implementing safeguards to protect the security and confidentiality of personal data that requires the adoption of administrative, physical and technical safeguards to protect such information, providing notification of data breaches to appropriate data protection authorities or data subjects, requiring data protection impact assessments for high risk processing and establishing means for data subjects to exercise rights in relation to their personal data and taking certain measures when engaging third-party processors. The GDPR's definition of personal data includes coded data. Failure to comply with the requirements of the GDPR may result in warning letters, mandatory audits, orders to cease/change the use of data, and financial penalties, including fines, which can be up to 4% of global revenues or €20 million (£17.5 million for the U.K.), whichever is greater. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR.

Among other requirements, the GDPR includes restrictions on cross-border transfers of personal data subject to the GDPR to countries outside the EEA/U.K. that have not been found to provide adequate protection to such personal data (third countries), unless a valid GDPR transfer mechanism (for example, the European Commission approved Standard Contractual Clauses, or SCCs, certification to the EU-U.S. Data Privacy Framework (which allows for transfers to relevant U.S.-based organizations who self-certify compliance and participate in the framework) and the U.K. International Data Transfer Agreement/Addendum, or U.K. IDTA) has been put in place. Where relying on the SCCs /U.K. IDTA for data transfers, we may also be required to carry out transfer impact assessments to assess whether the recipient is subject to local laws which allow public authority access to personal data. The international transfer obligations under the EEA/U.K. data protection regimes will require significant effort and cost and may result in us needing to make strategic considerations around where EEA/U.K. personal data is transferred and which service providers we can utilize for the processing of EEA/U.K. personal data. As supervisory authorities issue further guidance on personal data export mechanisms, including circumstances where the SCCs 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. Switzerland has also adopted similar restrictions on transfer of personal data outside of its borders. Although the U.K. is regarded as a third country under the EU's GDPR, the European Commission has adopted an (adequacy decision) in favor of the U.K., a decision recognizing the U.K. as providing adequate protection under the EU GDPR and enabling data transfers from EU Member States to the U.K. without additional safeguards. However, the U.K. adequacy decision will automatically expire in June 2025 unless the European Commission re-assesses and renews or extends that decision and remains under review by the Commission during this period. The U.K. government has confirmed that personal data transfers from the U.K. to the EEA remain free flowing. On October 24, 2024, the U.K. Government introduced its Data Use and Access Bill, or U.K. Bill, into the U.K. legislative process. If passed, the final version of the U.K. Bill may have the effect of further altering the similarities between the U.K. and EEA data protection regime and threaten the U.K. Adequacy Decision from the European Commission. This may lead to additional compliance costs and could increase our overall risk. It is unclear how U.K. data protection laws and regulations will develop in the medium to longer term, and how data transfers to and from the U.K. will be regulated in the long term. Although the EU GDPR and the U.K. GDPR currently impose substantially similar obligations it is possible that over time the respective provisions, interpretations and enforcement of the EU GDPR and U.K. GDPR may further diverge in the future and create additional regulatory challenges and uncertainties. The lack of clarity on future U.K. laws and regulations and their interaction with EU laws and regulations could add legal risk, uncertainty, complexity and cost to our handling of U.K. and EEA personal data and our privacy and data security compliance programs, and could require us to implement different compliance measures for the U.K. and the EEA.

If we are unable to implement a valid solution for personal data transfers from the EEA, U.K. or Switzerland to the U.S. or other countries, we will face increased exposure to regulatory actions, substantial fines and injunctions against processing personal data in those jurisdictions. Inability to import personal data from the EEA, U.K. or Switzerland may also restrict our clinical trials activities in those jurisdictions; limit our ability to collaborate with contract research organizations as well as other service providers, contractors and other companies subject to data protection laws in those jurisdictions; and require us to increase our data processing capabilities in those jurisdictions at significant expense. Additionally, other countries outside of the EEA, U.K., and Switzerland have enacted or are considering enacting similar cross-border data transfer restrictions and laws requiring local data residency, which could increase the cost and complexity of delivering our services and operating our business.

Given the breadth and depth of applicable data protection obligations, preparing for and complying with the GDPR and similar laws' requirements are rigorous and time intensive and require significant resources and a review of our technologies, systems and practices, as well as those of any third-party collaborators, service providers, contractors or consultants that process or transfer personal data. The GDPR, and other laws or regulations associated with the enhanced protection of certain types of sensitive data, such as healthcare data or other personal information from our clinical trials, could require us to change our business practices and put in place additional compliance mechanisms, may interrupt or delay our development, regulatory and commercialization activities and increase our cost of doing business, and could lead to government enforcement actions, private litigation and significant fines and penalties against us and could have a material adverse effect on our business, financial condition or results of operations.

Similar privacy and data security requirements are either in place or underway in the U.S. There are numerous data protection laws that may be applicable to our activities, and a range of enforcement agencies at both the state and federal levels that can review

companies for privacy and data security concerns based on general consumer protection laws. The Federal Trade Commission and state Attorneys General are aggressive in reviewing privacy and data security protections for consumers. New laws also are being considered or have been implemented at both the state and federal levels. For example, the California Consumer Privacy Act of 2018, or the CCPA, which became effective on January 1, 2020, requires companies that process information of California consumers (as defined under the CCPA) to provide disclosures to such consumers about their data collection, use and sharing practices, provides Californian consumers with new individual data privacy rights, imposes new operational requirements for covered businesses, provides a private right of action for data breaches and creates a statutory damages framework. Although there are limited exemptions for clinical trial data under the CCPA, the CCPA and other similar laws could impact our business activities depending on how such laws are interpreted. Additionally as of January 1, 2023, the California Privacy Rights Act, or CPRA has significantly modified the CCPA, including by expanding consumers' rights with respect to certain sensitive personal information. The CPRA also created a new state agency that will be vested with authority to implement and enforce the CCPA.

Many other states have enacted or are considering similar legislation, and a broad range of legislative measures also have been introduced at the federal level. Such proposed legislation, if enacted, may add additional complexity, variation in requirements, restrictions and potential legal risk, require additional investment of resources in compliance programs, impact strategies and the availability of previously useful data and could result in increased compliance costs and/or changes in business practices and policies. The existence of comprehensive privacy laws in different states in the country would make our compliance obligations more complex and costly and may increase the likelihood that we may be subject to enforcement actions or otherwise incur liability for noncompliance. There are also states that are specifically regulating health information. For example, Washington state recently passed a health privacy law that, as of June 30, 2024, regulates the collection and sharing of health information. This law also has a private right of action, which further increases the relevant compliance risk collecting the health information of Washington residents. Connecticut and Nevada have also passed similar laws regulating consumer health data. In addition, other states have proposed and/or passed legislation that regulates the privacy and/or security of certain specific types of information. For example, a small number of states have passed laws that regulate biometric data specifically. These various privacy and security laws may impact our business activities, including our identification of research subjects, relationships with business partners and ultimately the marketing and distribution of our products. State laws are changing rapidly and there is discussion in the U.S. Congress of a new comprehensive federal data privacy law to which we may likely become subject, if enacted.

Further, regulations promulgated pursuant to HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, and referred herein collectively as HIPAA, imposes privacy, security and breach notification obligations on health plans, healthcare clearinghouses and certain healthcare providers, known as covered entities, as well as their business associates that perform certain services that involve creating, receiving, maintaining or transmitting individually identifiable health information for or on behalf of such covered entities, and their covered subcontractors. HIPAA establishes privacy and security standards that limit the use and disclosure of protected health information, or PHI, and requires the implementation of administrative, physical and technological safeguards to protect the privacy of PHI and ensure the confidentiality, integrity and availability of electronic PHI. Most healthcare providers, including research institutions from which we obtain patient health information, are subject to HIPAA. We do not believe that we are currently acting as a covered entity or business associate under HIPAA and thus are not directly subject to its requirements. However, 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.

In addition to the risks associated with enforcement activities and potential contractual liabilities, our ongoing efforts to comply with evolving laws and regulations at the federal and state level may be costly and require ongoing modifications to our policies, procedures and systems. Further, any failure by our third-party collaborators, service providers, contractors or consultants to comply with applicable law, regulations or contractual obligations related to data privacy or security could result in proceedings against us by governmental entities or others.

We may also publish privacy policies and other documentation regarding our collection, processing, use and disclosure of personal information and/or other confidential information. Although we endeavor to comply with our published policies and other documentation, we may at times fail to do so or may be perceived to have failed to do so. Despite our efforts, we may not be successful in achieving compliance if our employees or vendors fail to comply with our published policies and documentation. Such failures can subject us to potential international, local, state and federal action if they are found to be deceptive, unfair, or misrepresentative of our actual practices.

All of these evolving compliance and operational requirements impose significant costs, such as costs related to organizational changes, implementing additional protection technologies, training employees and engaging consultants and legal advisors, which are likely to increase over time. In addition, such requirements may require us to modify our data processing practices and policies, utilize management's time and/or divert resources from other initiatives and projects. Claims that we have violated individuals' privacy rights or failed to comply with data protection laws or applicable privacy notices, even if we are not found liable, could be expensive and time-consuming to defend and could result in adverse publicity that could harm our business. Any failure or perceived failure by us to

comply with any applicable federal, state or foreign laws and regulations relating to data privacy and security could result in damage to our reputation, as well as proceedings or litigation by governmental agencies or other third parties, including consumer class actions related to these laws and the overall protection of personal information. Even if we are not determined to have violated these laws, government investigations into these issues typically require the expenditure of significant resources and generate negative publicity, which could harm our reputation and our business, financial condition, results of operations or prospects.

Further, the use of new and evolving technologies, such as artificial intelligence, in our business may result in spending material resources and presents risks and challenges that can impact our business including by posing security and other risks to our confidential and/or proprietary information, including personal information, and as a result we may be exposed to reputational harm and liability.

If any of our product candidates obtains regulatory approval and does not receive appropriate periods of non-patent exclusivity, competitors could enter the market with generic versions of such products more quickly than we expect, which may result in a material decline in sales of our products.

Under the Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Amendments to the FDCA, a company may file an abbreviated new drug application, or ANDA, seeking approval of a generic version of an approved innovator product. Under the Hatch-Waxman Amendments, a company may also submit an NDA under section 505(b)(2) of the FDCA that references the FDA's prior approval of the innovator product. A 505(b)(2) NDA product may be for a new or improved version of the original innovator product. The Hatch-Waxman Amendments also provide for certain periods of regulatory exclusivity, which preclude FDA approval (or in some circumstances, FDA filing and review) of an ANDA or 505(b)(2) NDA.

In the U.S., once an NDA is approved, the product covered thereby becomes a "reference listed drug" in the FDA's publication, "Approved Drug Products with Therapeutic Equivalence Evaluations," or the Orange Book. Manufacturers may seek approval of generic versions of reference listed drugs through submission of ANDAs in the U.S. In support of an ANDA, a generic manufacturer generally must show that its product has the same active ingredient(s), dosage form, strength, route of administration, and adequate labeling as the reference listed drug and that the generic version is bioequivalent to the reference listed drug, meaning, in part, that it is absorbed in the body at the same rate and to the same extent. Generic products may be significantly less costly to bring to market than the reference listed drug and companies that produce generic products are generally able to offer them at lower prices. Moreover, many states allow or require substitution of therapeutically equivalent generic drugs at the pharmacy level even if the branded drug is prescribed. Thus, following the introduction of a generic drug, a significant percentage of the sales of any branded product or reference listed drug may be lost to the generic product.

The FDA may not finally approve an ANDA for a generic product until any applicable period of non-patent exclusivity for the reference listed drug has expired. The FDCA provides a period of five years of non-patent exclusivity for a new drug containing a NCE. For the purposes of this provision, an NCE is a drug that contains no active moiety that has previously been approved by the FDA in any other NDA. An active moiety is the molecule or ion responsible for the physiological or pharmacological action of the drug substance. Specifically, in cases where such exclusivity has been granted, an ANDA may not be filed with the FDA until the expiration of five years unless the submission is accompanied by a patent certification that a patent covering the listed drug is invalid unenforceable or will not be infringed by the generic product. In that case, the applicant may submit its application four years following approval of the listed drug and seek to launch its generic product even if we still have patent protection for our product unless an infringement suit is timely filed by the NDA or patent holder in which case the FDA cannot approve the ANDA for 30 months unless a court decision in favor of the generic manufacturer is issued earlier.

Three-year exclusivity is given to a drug if it contains an active moiety that has previously been approved, and the NDA includes reports of one or more new clinical investigations, other than bioavailability or bioequivalence studies, that were conducted by or for the applicant and are essential to the approval of the NDA. This form of marketing exclusivity is known as New Clinical Investigation, or NCI, exclusivity. If our product candidates are approved with only NCI exclusivity, generic manufacturers may file their ANDAs any time following approval of our product candidates and seek to launch their generic products following the expiration of the three year market exclusivity period, even if we still have patent protection for our product unless an infringement suit is timely filed triggering a 30 month stay on approval of the generic product (subject to the disposition of the patent litigation).

While we believe that our product candidates may be NCEs in the U.S., the FDA may determine, however, that they are not eligible for NCE exclusivity but receive three years of NCI exclusivity instead, if and when FDA approves an NDA for the product. If any product we develop does not receive five years of NCE exclusivity, the FDA may approve generic versions of such product three years after its date of approval, subject to any patents exclusivity we may have. If an ANDA applicant certifies to the invalidity or non-infringement of listed patents and an infringement suit is timely filed by the NDA or patent holder, the FDA cannot finally approve the ANDA for 30 months unless a court decision in favor of the generic manufacturer is issued earlier.

Accordingly, if any of our product candidates is approved, competitors could file ANDAs for generic versions of these products or 505(b)(2) NDAs that reference our product candidates. If there are patents listed for our product candidates in the Orange Book, any ANDA and 505(b)(2) NDA applicants would be required to include a certification as to each listed patent indicating whether the

ANDA applicant does or does not intend to challenge the patent. FDORA also requires that the FDA consider therapeutic equivalence determinations for certain Section 505(b)(2) drugs that are pharmaceutical equivalents to listed drugs relied upon in an application either at the time of approval or up to 180 days post-approval, upon request of the sponsor. These therapeutic equivalence determinations could have an adverse effect on our business. Because we remain early in the research and preclinical development of our product candidates, we cannot predict which, if any, patents in our current portfolio or patents we may obtain in the future will be eligible for listing in the Orange Book, how any generic competitor would address such patents, whether we would sue on any such patents or the outcome of any such suit.

We may not be successful in securing or maintaining proprietary patent protection for products and technologies we develop or license, despite expending a significant amount of resources that could have been focused on other areas of our business. Moreover, if any of our owned or in-licensed patents that are listed in the Orange Book are successfully challenged by way of a patent certification and subsequent litigation, the affected product could immediately face generic competition and its sales would likely decline rapidly and materially.

Risks Related to Commercialization

We face substantial competition, which may result in others discovering, developing or commercializing products before us or more successfully than we do.

The development and commercialization of new drug products is highly competitive. We face competition with respect to our product candidates from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide. 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 many of the disorders for which we are conducting research programs. Some of these competitive products and therapies are based on scientific approaches that are the same as or similar to our approach, and others are based on entirely different approaches. 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.

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 our product candidates or that would render our product candidates obsolete or non-competitive. Our competitors also may obtain FDA, EMA 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. Additionally, technologies developed by our competitors may render our potential product candidates uneconomical or obsolete, and we may not be successful in marketing our product candidates against competitors.

We expect to face competition from existing products and product candidates in development for each of our programs. Currently, patients with DMD are treated with corticosteroids to manage the inflammatory component of the disease. EMFLAZA is an FDA-approved corticosteroid marketed by PTC. Individuals with DMD also use prednisone or prednisolone off-label. In addition, there are several FDA-approved exon skipping drugs: EXONDYS 51 and VYONDYS 53, which are naked PMOs approved for the treatment of DMD patients amenable to exon 51 and exon 53 skipping, respectively, and are marketed by Sarepta; and VILTEPSO, a naked PMO approved for the treatment of DMD patients amenable to exon 53 skipping, which is marketed in the U.S. by NS Pharma, Inc. Notably, it was reported in May 2024 that the Phase 3, confirmatory study of VILTEPSO failed to meet the primary endpoint, Time to Stand from Supine, measured as velocity rise per second. Companies focused on developing treatments for DMD that target dystrophin production, as our DMD program does, include Dyne, with DYNE-251, an antibody-conjugated PMO that targets exon 51 skipping in a Phase 1/2 clinical trial; BioMarin, with BMN-351, a phosphorothioate oligonucleotide that targets exon 51 skipping currently in preclinical development; and Wave, with WVE-N531, a stereopure oligonucleotide in a Phase 1/2 clinical trial for patients amenable to exon 53 skipping. In November 2024, Sarepta announced it was discontinuing development of SRP-5051, a peptide-linked PMO for patients amenable to exon 51 skipping due to certain adverse events experienced by patients.

In addition, several companies are developing gene therapies to treat DMD. These include ELEVIDYS, which was approved in June 2023 for treatment of ambulatory pediatric patients aged 4 through 5 years with DMD with a confirmed mutation in the DMD gene. In June 2024, the FDA granted approval of an expansion to the labeled indication for ELEVIDYS to include individuals with DMD with a confirmed mutation in the DMD gene who are at least 4 years of age, granting traditional approval for ambulatory patients and accelerated approval for non-ambulatory patients. Continued approval for non-ambulatory DMD patients may be contingent upon verification of clinical benefit in a confirmatory trial. In addition, several other companies are developing investigational gene therapies to treat DMD, including Solid Biosciences Inc.'s SGT-003 and REGENXBIO Inc.'s RGX-202, currently in Phase 1 and Phase 2 clinical development, respectively. Gene editing treatments that are in preclinical development are also being pursued by Vertex and Sarepta. We are also aware of several companies targeting non-dystrophin mechanisms for the treatment of DMD, including Edgewise with EDG-5506, a muscle stabilizer that is currently in clinical development and Italfarmaco

S.p.A., with Duvyzat, an oral histone deacetylase, or HDAC inhibitor, that reduces fibrosis in patients with DMD and was approved by the FDA in March of 2024 for the treatment of DMD in patients six years of age and older, and is under review by the EMA.

For DM1, there are currently no approved therapies to treat the underlying cause of the disease. Pipeline candidates currently in development to treat DM1 include several approaches that target DMPK RNA. These include AOC 1001, an antibody linked siRNA in Phase 3 clinical development by Avidity; DYNE-101, an antibody conjugated antisense oligonucleotide in Phase 1/2 clinical development by Dyne; VX-670, a peptide conjugated PMO in Phase 2 by Entrada and Vertex; and ARO-DM1, a conjugated siRNA in Phase 1/2 clinical development by Arrowhead and Sarepta. There are additional approaches under development such as ATX-01, a microRNA that modulates expression of MBNL1 by Arthex Biotech S.L., that is in Phase 1 clinical development. Another small molecule, tideglusib, which is a GSK3- β inhibitor is in clinical development by AMO for the congenital phenotype of DM1.

Several gene editing and gene delivery treatments are in discovery or preclinical development by Vertex and Kate Therapeutics Inc. (recently acquired by Novartis); Design is developing an approach to prevent formation of CUG hairpins; Expansion and Arrakis are developing an approach utilizing the interaction of small molecules with RNA in preclinical development; and therapeutics based on biomolecular condensate biology in preclinical development by Dewpoint and Pfizer.

We will also compete more generally with other companies developing alternative scientific and technological approaches, including other companies working to develop conjugates with oligonucleotides for extra-hepatic delivery, including Alnylam, Aro, Arrowhead, Avidity, Dicerna Pharmaceuticals, Inc. (acquired by Novo Nordisk), Dyne, Entrada, Ionis, NeuBase, PYC and Sarepta, as well as gene therapy and gene editing approaches.

Many of the companies against which we compete or against which we may compete in the future 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. Accordingly, our competitors may be more successful than us in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining approval for treatments and achieving widespread market acceptance, rendering our treatments obsolete or non-competitive.

Additionally, 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 and other early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

If we successfully obtain approval for any product candidate, we will face competition based on many different factors, including the safety and effectiveness of our products, the ease with which our products can be administered and the extent to which patients accept relatively new routes of administration, the timing and scope of regulatory approvals for these products, the availability and cost of manufacturing, marketing and sales capabilities, price, reimbursement coverage and patent position. Competing products could present superior treatment alternatives, including by being more effective, safer, more convenient, less expensive or marketed and sold more effectively than any of our products, if approved. Competitive products or technological approaches may make any products we develop, or our EDO platform, obsolete or noncompetitive before we recover the expense of developing and commercializing our product candidates. If we are unable to compete effectively, our opportunity to generate revenue from the sale of our products, if approved, could be adversely affected.

Even if one or more of our product candidates receives marketing approval, it may fail to achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success.

If any of our product candidates progresses successfully through clinical development and receives marketing approval, it may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. Sales of medical products depend in part on the willingness of physicians to prescribe the treatment, which is likely to be based on a determination by these physicians that the products are safe, therapeutically effective and cost-effective. In addition, the inclusion or exclusion of products from treatment guidelines established by various physician groups and the viewpoints of influential physicians can affect the willingness of other physicians to prescribe the treatment. We cannot predict whether physicians, physicians' organizations, hospitals, other healthcare providers, government agencies or private insurers will determine that our product is safe, therapeutically effective and cost-effective as compared with competing treatments. Efforts to educate the medical community and third-party payors on the benefits of our product candidates may require significant resources and may not be successful. If our product candidates do not achieve an adequate level of acceptance, we may not generate significant product revenues and we may not become profitable. The degree of market acceptance of our product candidates, if approved for commercial sale, will depend on a number of factors, including:

- the efficacy and safety of such product candidates as demonstrated in clinical trials;
- the potential advantages and limitations compared to alternative treatments;

- the effectiveness of sales and marketing efforts;
- the cost of treatment in relation to alternative treatments;
- the clinical indications for which the product is approved;
- the convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the strength of marketing and distribution support;
- the timing of market introduction of competitive products;
- the availability of third-party coverage and adequate reimbursement;
- the prevalence and severity of any side effects; and
- any restrictions on the use of our products, if approved, together with other medications.

If the market opportunities for any product candidates we develop are smaller than we believe they are, our revenue may be adversely affected, and our business may suffer. Because the target patient populations of our programs are small, and the addressable patient population even smaller, we must be able to successfully identify patients and capture a significant market share to achieve profitability and growth.

We focus our research and product development on treatments for rare diseases. Given the small number of patients who have the diseases that we are targeting, it is critical to our ability to grow and become profitable that we continue to successfully identify patients with these rare diseases. Our 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 our product candidates, are based on our beliefs and estimates. These estimates have been derived from a variety of sources, including the scientific literature, surveys of clinics, patient foundations or market research that we conducted, and may prove to be incorrect or contain errors. New studies may change the estimated incidence or prevalence of these diseases. The number of patients may turn out to be lower than expected. The effort to identify patients with diseases we seek to treat is in early stages, and we cannot accurately predict the number of patients for whom treatment might be possible. Additionally, the potentially addressable patient population for each of our product candidates may be limited or may not be amenable to treatment with our product candidates, and new patients may become increasingly difficult to identify or gain access to, which would adversely affect our results of operations and our business. Further, even if we obtain significant market share for our product candidates, because the potential target populations are very small, we may never achieve profitability despite obtaining such significant market share.

Our target patient populations are relatively small, and as a result, the pricing and reimbursement of our product candidates, if approved, is uncertain, but must be adequate to support commercial infrastructure. If we are unable to obtain adequate levels of reimbursement, our ability to successfully market and sell product candidates will be adversely affected.

The estimates of market opportunity and forecasts of market growth included in this 10-K, if any, may prove to be inaccurate, and even if the markets in which we compete achieve the forecasted growth, our business may not grow at similar rates, or at all.

Market opportunity estimates and growth forecasts included in this 10-K, if any, are subject to significant uncertainty and are based on assumptions and estimates which may not prove to be accurate. The estimates and forecasts included in this 10-K relating to size and expected growth of our target market, if any, may prove to be inaccurate. Even if the markets in which we compete meet any size estimates and/or growth forecasts included in this 10-K, our business may not grow at similar rates, or at all. Our growth is subject to many factors, including our success in implementing our business strategy, which is subject to many risks and uncertainties.

The pricing and third-party payor coverage and reimbursement status of newly approved products are uncertain. Failure to obtain or maintain adequate coverage and reimbursement for our future product candidates, if approved, could limit our ability to market those products and decrease our ability to generate product revenue.

In the U.S. and markets in other countries, patients generally rely on third-party payors to reimburse all or part of the costs associated with their treatment. Adequate coverage and reimbursement from governmental healthcare programs, such as Medicare and Medicaid, and commercial payors is critical to new product acceptance. Our ability to successfully commercialize our product candidates will depend in part on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers and other organizations. 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. Even if coverage is provided, the approved reimbursement amount may

not be high enough to allow us to establish or maintain pricing sufficient to realize a sufficient return on our investment. For more information, see “*Business – Healthcare Regulation – Coverage and Reimbursement*” in this 10-K.

Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. There is significant uncertainty related to the insurance coverage and reimbursement of newly approved products. In the U.S., the decisions about coverage and reimbursement for new products under the Medicare program are made by the Centers for Medicare & Medicaid Services, or CMS. Private payors tend to follow CMS to a substantial degree. However, one payor’s determination to provide coverage for a product does not assure that other payors will also provide coverage for the drug product. Further, a payor’s decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Reimbursement agencies in the EU may be more conservative than CMS. Factors payors consider in determining reimbursement are based on whether the product is:

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

Additionally, net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the U.S. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. We cannot be sure that reimbursement will be available for any product candidate that we commercialize and, if reimbursement is available, the level of reimbursement. In addition, many pharmaceutical manufacturers must calculate and report certain price reporting metrics to the government, such as average sales price, or ASP, and best price. Penalties may apply in some cases when such metrics are not submitted accurately and timely. Further, these prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs.

Outside the U.S., 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 the EU, the U.K., Canada and other countries has and will continue to put pressure on the pricing and usage of therapeutics such as our product candidates. In many countries, particularly the countries of the EU, the prices of medical products are subject to varying price control mechanisms as part of national health systems. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. As a result, we might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay or might even prevent our commercial launch of the product, possibly for lengthy periods of time. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidate to other available therapies. In general, the prices of products under such systems are substantially lower than in the U.S. Other countries allow companies to fix their own prices for products but monitor and control company profits. Additional foreign price controls or other changes in pricing regulation could restrict the amount that we are able to charge for product candidates. Accordingly, in markets outside the U.S., the reimbursement for our product candidates may be reduced compared with the U.S. and may be insufficient to generate commercially reasonable revenues and profits.

If we are unable to establish sales, marketing and distribution capabilities or enter into sales, marketing and distribution agreements with third parties, we may not be successful in commercializing our product candidates if any are approved.

We do not have a sales or marketing infrastructure and have no experience in the sale, marketing or distribution of pharmaceutical products. To achieve commercial success for any product for which we have obtained marketing approval, we will need to establish a sales, marketing and distribution organization, either ourselves or through collaborations or other arrangements with third parties.

In the future, we may build a sales and marketing infrastructure to market certain of our product candidates if they receive marketing approval. There are risks involved with establishing our own sales, marketing and distribution capabilities. For example, recruiting and training a sales force is expensive and time-consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. These efforts may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

Factors that may inhibit our efforts to commercialize our products on our own include:

- our inability to recruit, train and retain adequate numbers of effective sales, marketing, coverage or reimbursement, customer service, medical affairs and other support personnel;
- the inability of sales personnel to educate adequate numbers of physicians on the benefits of any future products;
- the inability of reimbursement professionals to negotiate arrangements for formulary access, reimbursement and other acceptance by payors;
- the inability to price our products at a sufficient price point to ensure an adequate and attractive level of profitability;
- restricted or closed distribution channels that make it difficult to distribute our products to segments of the patient population;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

If we are unable to establish our own sales, marketing and distribution capabilities and we enter into arrangements with third parties to perform these services, our product revenues and our profitability, if any, are likely to be lower than if we were to market, sell and distribute any products that we develop ourselves. In addition, we may not be successful in entering into arrangements with third parties to sell, market and distribute our product candidates or may be unable to do so on terms that are acceptable to us. We likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively. If we do not establish sales, marketing and distribution capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates.

Risks Related to Our Intellectual Property

If we or our licensors are unable to obtain, maintain and defend patent and other intellectual property protection for any product candidates or technology, or if the scope of the patent or other intellectual property protection obtained is not sufficiently broad, our competitors could develop and commercialize products and technology similar or identical to ours, and our ability to successfully develop and commercialize our product candidates or our technology may be adversely affected due to such competition.

Our success depends in large part on our and our licensors' ability to obtain and maintain patent and other intellectual property protection in the U.S. and other jurisdictions. We and our licensors have sought, and will seek, to protect our proprietary position by filing additional patent applications in the U.S. and abroad related to certain technologies and our platform that are important to our business. However, our patent portfolio is at a somewhat early stage; there are two issued patents (one of which is a European patent validated in five countries), which we in-licensed from Oxford University Innovation Limited, or OUI, and the Medical Research Council of United Kingdom Research and Innovation, or MRC, and substantive examination of more than half of the currently pending patent applications we own or license has yet to begin. In addition, there can be no assurance as to whether or when our patent applications will issue as granted patents. Our ability to stop third parties from making, using, selling, marketing, offering to sell, importing and commercializing our product candidates and our technology is dependent upon the extent to which we have rights under valid and enforceable patents and other intellectual property that cover our platform and technology. If we are unable to secure, maintain, defend and enforce patents and other intellectual property with respect to our product candidates and our technology, it would have a material adverse effect on our business, financial condition, results of operations and prospects.

Our pending PCT patent applications are not eligible to become issued patents until, among other things, we file a national stage patent application within 30 to 32 months, depending on the jurisdiction, from such application's priority date in the jurisdictions in which we are seeking patent protection. Similarly, our pending provisional patent applications are not eligible to become issued patents until, among other things, we file a non-provisional patent application within 12 months of such provisional patent application's filing date. If we do not timely file such national stage patent applications or non-provisional patent applications, we may lose our priority date with respect to such PCT or provisional patent applications, respectively, and any patent protection on the inventions disclosed in such PCT or provisional patent applications, respectively. While we and our licensors intend to timely file national stage and non-provisional patent applications relating to our PCT and provisional patent applications, respectively, we cannot predict whether any such patent applications will result in the issuance of patents. If we or our licensors do not successfully obtain issued patents, or, if the scope of any patent protection we or our licensors obtain is not sufficiently broad, we will be unable to prevent others from using our product candidates or our technology or from developing or commercializing technology and products similar or identical to ours or other competing products and technologies. Any failure to obtain or maintain patent protection with respect to our product candidates or our EDO platform would have a material adverse effect on our business, financial condition, results of operations and prospects.

The patent prosecution process is expensive, time-consuming and complex, and we and our licensors may not be able to file, prosecute, maintain, defend, enforce or license all necessary or desirable patent applications at a reasonable cost or in a timely manner. We and our licensors may not be able to obtain, maintain or defend patents and patent applications due to the subject matter claimed in such patents and patent applications being in the public domain. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Although we enter into non-disclosure and confidentiality agreements with parties who have access to confidential or patentable aspects of our research and development output, such as our employees, corporate collaborators, outside scientific collaborators, contract manufacturers, consultants, advisors and other third parties, any of these parties may breach these agreements and disclose such output before a patent application is filed, thereby jeopardizing our ability to seek patent protection. Consequently, we would not be able to prevent any third party from using any of our technology that is in the public domain to compete with our product candidates.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has, in recent years, been the subject of much litigation. As a result, the issuance, scope, validity, enforceability and commercial value of patent rights are highly uncertain. Our pending and future owned and licensed patent applications may not result in patents being issued which protect our technology or product candidates, effectively prevent others from commercializing competitive technologies and product or otherwise provide any competitive advantage. In fact, patent applications may not issue as patents at all, and even if such patent applications do issue as patents, they may not issue in a form, or with a scope of claims, that will provide us with any meaningful protection, prevent others from competing with us or otherwise provide us with any competitive advantage. In addition, the scope of claims of an issued patent can be reinterpreted after issuance, and changes in either the patent laws or interpretation of the patent laws in the U.S. and other jurisdictions may diminish the value of our patent rights or narrow the scope of our patent protection. Furthermore, our competitors or other third parties may be able to circumvent our patents by developing similar or alternative technologies or products in a non-infringing manner.

Third parties have developed technologies that may be related or competitive to our own technologies and product candidates and may have filed or may file patent applications, or may have obtained issued patents, claiming inventions that may overlap or conflict with those claimed in our owned or licensed patent applications or issued patents. We may not be aware of all third-party intellectual property rights potentially relating to our current and future product candidates and technology. Publications of discoveries in the scientific literature often lag the actual discoveries, and patent applications in the U.S. and other jurisdictions are typically not published until 18 months after filing or, in some cases, not at all. Therefore, we cannot know for certain whether the inventors of our owned or licensed patents and patent applications were the first to make the inventions claimed in any owned or licensed patents or pending patent applications, or that we were the first to file for patent protection of such inventions. If a third party can establish that we or our licensors were not the first to make or the first to file for patent protection of such inventions, our owned or licensed patent applications may not issue as patents and even if issued, may be challenged and invalidated or ruled unenforceable.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our owned and licensed patents may be challenged in the courts or patent offices in the U.S. and other jurisdictions. For example, we may be subject to a third-party submission of prior art to the USPTO, challenging the validity of one or more claims of our owned or licensed patents. Such submissions may also be made prior to a patent's issuance, precluding the granting of a patent based on one of our owned or licensed pending patent applications. We may become involved in opposition, derivation, re-examination, inter partes review, post-grant review or interference proceedings and similar proceedings in foreign jurisdictions (for example, opposition proceedings) challenging our owned or licensed patent rights. In addition, a third party may claim that our owned or licensed patent rights are invalid or unenforceable in a litigation. An adverse result in any litigation or patent office proceeding could put one or more of our owned or licensed patents at risk of being invalidated, ruled unenforceable or interpreted narrowly and could allow third parties to commercialize products identical or similar to our product candidates and compete directly with us, without payment to us. Moreover, we, or one of our licensors, may have to participate in interference proceedings declared by the USPTO to determine priority of invention or in post-grant challenge proceedings, such as oppositions in a foreign patent office, that challenge priority of invention or other features of patentability. Such challenges and proceedings may result in loss of patent rights, exclusivity or in patent claims being narrowed, invalidated or held unenforceable, 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 our product candidates. Such challenges and proceedings may also result in substantial cost and require significant time from our scientists and management, even if the eventual outcome is favorable to us. Moreover, there could be public announcements of the results of hearings, motions or other interim proceedings or developments related to such challenges and proceedings. If securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock.

Furthermore, patents have a limited lifespan. In the U.S., the expiration of a patent is generally 20 years from the earliest date of filing of the first non-provisional patent application to which the patent claims priority. Patent term adjustments and extensions may be available; however, the overall term of a patent, and the protection it affords, is limited. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such product candidates might expire before or shortly after such product candidates are commercialized. As a result, our owned and licensed patent and other intellectual property rights may not provide us with sufficient rights to exclude others from commercializing products similar or identical to our technology

and our product candidates. Any of the foregoing could have a material adverse effect on our competitive position, business, financial condition, results of operations and prospects.

Our rights to develop and commercialize any product candidates are subject and may in the future be subject, in part, to the terms and conditions of licenses granted to us by third parties. If we fail to comply with our obligations under our current or future intellectual property license agreements or otherwise experience disruptions to our business relationships with our current or any future licensors, we could lose intellectual property rights that are important to our business.

We are and expect to continue to be reliant upon third-party licensors for certain patent and other intellectual property rights that are important or necessary to the development of our technology and product candidates. For example, we rely on a license from OUI and MRC, to certain patent rights and know-how of OUI and MRC. The OUI/MRC License imposes, and we expect that any future license agreement will impose, specified diligence, milestone payment, fee payment, royalty, commercialization, development and other obligations on us and require us to meet development timelines, or to exercise diligent or commercially reasonable efforts to develop and commercialize licensed products, in order to maintain the licenses.

Furthermore, our licensors have, or may in the future have, the right to terminate a license if we materially breach the agreement and fail to cure such breach within a specified period or in the event we undergo certain bankruptcy events. In spite of our best efforts, our current or any future licensors might conclude that we have materially breached our license agreements and might therefore terminate the license agreements. If our license agreements are terminated, we may lose our rights to develop and commercialize product candidates and technology, lose patent protection, experience significant delays in the development and commercialization of our product candidates and technology, and incur liability for damages. If these in-licenses are terminated, or if the underlying intellectual property fails to provide the intended exclusivity, our competitors or other third parties could have the freedom to seek regulatory approval of, and to market, products and technologies identical or competitive to ours and we may be required to cease our development and commercialization of certain of our product candidates and technology. In addition, we may seek to obtain additional licenses from our licensors and, in connection with obtaining such licenses, we may agree to amend our existing licenses in a manner that may be more favorable to the licensors, including by agreeing to terms that could enable third parties, including our competitors, to receive licenses to a portion of the intellectual property that is subject to our existing licenses and to compete with our product candidates and our technology. Any of the foregoing could have a material adverse effect on our competitive position, business, financial condition, results of operations and prospects.

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

- the scope of rights granted under the license agreement and other interpretation-related issues;
- our or our licensors' ability to obtain, maintain and defend intellectual property and to enforce intellectual property rights against third parties;
- the extent to which our technology, product candidates and processes infringe, misappropriate or otherwise violate the intellectual property of the licensor that is not subject to the license agreement;
- the sublicensing of patent and other intellectual property rights under our license agreements;
- our diligence, development, regulatory, commercialization, financial or other obligations under the license agreement and what activities satisfy those diligence obligations;
- the inventorship and ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our current or future licensors and us and our partners; and
- the priority of invention of patented technology.

In addition, the OUI/MRC License is, and future license agreements are likely to be, complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology, or increase what we believe to be our diligence, development, regulatory, commercialization, financial or other obligations under the relevant agreement. In addition, if disputes over intellectual property that we have licensed or any other dispute related to our license agreements prevent or impair our ability to maintain our license agreements on commercially acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates and technology. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

While the OUI/MRC License grants certain exclusive patent and technology rights to us, license agreements we may enter into in the future may be non-exclusive. Accordingly, third parties may also obtain non-exclusive licenses from such licensors with respect to the intellectual property licensed to us under such license agreements. Accordingly, these license agreements may not provide us with exclusive rights to use such licensed patent and other intellectual property rights, or may not provide us with exclusive rights to

use such patent and other intellectual property rights in all relevant fields of use and in all territories in which we may wish to develop or commercialize our technology and our product candidates.

Moreover, some of our in-licensed patent and other intellectual property rights are, and may in the future be, subject to third party interests such as co-ownership. If we are unable to obtain an exclusive license to such third-party co-owners' interest, in such patent and other intellectual property rights, such third-party co-owners may be able to license their rights to other third parties, including our competitors, and our competitors could market competing products and technology. We or our licensors may need the cooperation of any such co-owners of our licensed patent and other intellectual property rights in order to enforce them against third parties, and such cooperation may not be provided to us or our licensors.

Additionally, we may not have complete control over the preparation, filing, prosecution, maintenance, enforcement and defense of patents and patent applications that we license from third parties. It is possible that our licensors' filing, prosecution and maintenance of the licensed patents and patent applications, enforcement of patents against infringers or defense of such patents against challenges of validity or claims of enforceability may be less vigorous than if we had conducted them ourselves, and accordingly, we cannot be certain that these patents and patent applications will be prepared, filed, prosecuted, maintained, enforced and defended in a manner consistent with the best interests of our business. If our licensors fail to file, prosecute, maintain, enforce and defend such patents and patent applications, or lose rights to those patents or patent applications, the rights we have licensed may be reduced or eliminated, our right to develop and commercialize any of our technology and any product candidates we may develop that are the subject of such licensed rights could be adversely affected and we may not be able to prevent competitors or other third parties from making, using and selling competing products.

Furthermore, our owned and in-licensed patent rights may be subject to a reservation of rights by one or more third parties. When new technologies are developed with government funding, in order to secure ownership of patent rights related to the technologies, the recipient of such funding is required to comply with certain government regulations, including timely disclosing the inventions claimed in such patent rights to the U.S. or foreign government and timely electing title to such inventions. A failure to meet these obligations may lead to a loss of rights or the unenforceability of relevant patents or patent applications.

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

Filing, prosecuting, maintaining, enforcing and defending patents and other intellectual property rights on our technology and our product candidates in all jurisdictions throughout the world would be prohibitively expensive, and accordingly, our intellectual property rights in some jurisdictions outside the U.S. could be less extensive than those in the U.S. In some cases, we or our licensors may not be able to obtain patent or other intellectual property protection for certain technology and product candidates outside the U.S. In addition, the laws of some foreign jurisdictions do not protect intellectual property rights to the same extent as federal and state laws in the U.S. Consequently, we and our licensors may not be able to obtain issued patents or other intellectual property rights covering our product candidates and our technology in all jurisdictions outside the U.S. and, as a result, may not be able to prevent third parties from practicing our and our licensors' inventions in all countries outside the U.S., or from selling or importing products made using our inventions in and into the U.S. or other jurisdictions. Third parties may use our technologies in jurisdictions where we and our licensors have not pursued and obtained patent or other intellectual property protection to develop their own products and, further, may export otherwise infringing, misappropriating or violating products to territories where we have patent or other intellectual property protection, but enforcement is not as strong as that in the U.S. These products may compete with our product candidates and our technology and our or our licensors' patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Additionally, many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain jurisdictions, particularly certain developing countries, do not favor the enforcement of patents, trade secrets and other intellectual property protection, particularly those relating to biotechnology products, which could make it difficult for us to stop the infringement, misappropriation or other violation of our patent and other intellectual property rights or marketing of competing products in violation of our intellectual property rights generally. For example, an April 2019 report from the Office of the U.S. Trade Representative identified a number of countries, including China, Russia, Argentina, Chile and India, where challenges to the procurement and enforcement of patent rights have been reported. Proceedings to enforce our or our licensors' patent and other intellectual property rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patent and other intellectual property rights at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We or our licensors may not prevail in any lawsuits that we or our licensors initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Many jurisdictions have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, many jurisdictions limit the enforceability of patents against government agencies or government contractors. In these jurisdictions, the patent owner may have limited remedies, which could materially diminish the value of such patents. If we or

any of our licensors is forced to grant a license to third parties with respect to any patents relevant to our business, our competitive position may be impaired, and our business, financial condition, results of operations and prospects may be adversely affected.

We may be involved in lawsuits to protect or enforce our patents or other intellectual property or the intellectual property of our licensors, which could be expensive, time-consuming, and unsuccessful.

Competitors may infringe our patents or other intellectual property or the intellectual property of our licensors. To cease such infringement or unauthorized use, we may be required to file patent infringement claims, which can be expensive and time-consuming and divert the time and attention of our management and scientific personnel. Our pending patent applications cannot be enforced against third parties practicing the technology claimed in such applications unless and until a patent issues from such applications. In addition, in an infringement proceeding or a declaratory judgment action, a court may decide that one or more of our patents is not valid or is unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation or defense proceeding could put one or more of our patents at risk of being invalidated, held unenforceable, or interpreted narrowly and could put our patent applications at risk of not issuing. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business.

Even if we establish infringement, the court may decide not to grant an injunction against further infringing activity and instead award only monetary damages, which may or may not be an adequate remedy. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock.

Changes in patent law in the U.S. or worldwide could diminish the value of patents in general, thereby impairing our ability to protect our product candidates and our technology.

Changes in either the patent laws or interpretation of patent laws in the U.S. and worldwide, including patent reform legislation such as the Leahy-Smith America Invents Act, or Leahy-Smith Act, could increase the uncertainties and costs surrounding the prosecution of any owned or in-licensed patent applications and the maintenance, enforcement or defense of any current in-licensed issued patents and issued patents we may own or in-license in the future. The Leahy-Smith Act includes a number of significant changes to U.S. patent law. These changes include provisions that affect the way patent applications are prosecuted, redefine prior art, provide more efficient and cost-effective avenues for competitors to challenge the validity of patents, and enable third-party submission of prior art to the USPTO during patent prosecution and additional procedures to attack the validity of a patent at USPTO-administered post-grant proceedings, including post-grant review, inter partes review, and derivation proceedings. Assuming that other requirements for patentability are met, prior to March 2013, in the U.S., the first to invent the claimed invention was entitled to the patent, while outside the U.S., the first to file a patent application was entitled to the patent. After March 2013, under the Leahy-Smith Act, the U.S. transitioned to a first-to-file system in which, assuming that the other statutory requirements for patentability are met, the first inventor to file a patent application will be entitled to the patent on an invention regardless of whether a third party was the first to invent the claimed invention. As such, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our in-licensed issued patents and issued patents we may own or in-license in the future, all of which could have a material adverse effect on our business, financial condition, results of operations and prospects. Since patent applications in the U.S. and most other countries are confidential for a period of time after filing or until issuance, we cannot be certain that we or our licensors were the first to either (i) file any patent application related to our product candidates or (ii) invent any of the inventions claimed in our or our licensor's patents or patent applications.

The America Invents Act also includes a number of significant changes that affect the way patent applications will be prosecuted and also may affect patent litigation. These include allowing third party submission of prior art to the USPTO during patent prosecution and additional procedures to attack the validity of a patent by USPTO administered post-grant proceedings, including post-grant review, inter partes review, and derivation proceedings. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in U.S. federal courts necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim unpatentable 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 review patentability of our patent claims that would not have been invalidated if first challenged by the third party as a defendant in a district court action. Therefore, the America Invents Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our owned or in-licensed patent applications and the enforcement or defense of our owned or in-licensed issued patents, all of which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

In addition, the patent positions of companies in the development and commercialization of pharmaceuticals are particularly uncertain. Recent U.S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. As one example, in the case *Assoc. for Molecular Pathology v. Myriad Genetics, Inc.*, the U.S. Supreme Court held that certain claims to DNA molecules are not patentable simply because they have been isolated from surrounding material. Moreover, in 2012, the USPTO issued a guidance memo to patent examiners indicating that process claims directed to a law of nature, a natural phenomenon or a naturally occurring relation or correlation that do not include additional elements or steps that integrate the natural principle into the claimed invention such that the natural principle is practically applied and the claim amounts to significantly more than the natural principle itself should be rejected as directed to patent-ineligible subject matter. Accordingly, in view of the guidance memo, there can be no assurance that claims in our patent rights covering our product candidates or our technology will be held by the USPTO or equivalent foreign patent offices or by courts in the U.S. or in foreign jurisdictions to cover patentable subject matter. This combination of events has created uncertainty with respect to the validity and enforceability of patents once obtained. Depending on future actions by the U.S. Congress, the federal courts and the USPTO, the laws and regulations governing patents could change in unpredictable ways that could have a material adverse effect on our patent rights and our ability to protect, defend and enforce our patent rights in the future.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by government patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

Periodic maintenance fees, renewal fees, annuity fees and various other government fees on patents and/or patent applications will be due to be paid to the USPTO and various government patent agencies outside of the U.S. over the lifetime of our owned or licensed patent rights. We rely on our outside counsel and other professionals or our licensing partners to pay these fees due to the USPTO and non-U.S. government patent agencies. The USPTO and various non-U.S. government patent agencies also require compliance with several procedural, documentary and other similar provisions during the patent application process. We rely on our outside counsel and other professionals to help us comply and we are also dependent on our licensors to take the necessary action to comply with these requirements with respect to our licensed intellectual property. In many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. There are situations, however, in which non-compliance can result in abandonment, loss of priority or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, potential competitors might be able to enter the market and this circumstance could have a material adverse effect on our competitive position, business, financial condition, results of operations and prospects.

We may not be successful in obtaining necessary rights to our product candidates through acquisitions and in-licenses.

We currently have rights to certain intellectual property through the OUI/MRC License. Because our programs may require the use of additional intellectual property rights held by third parties, the growth of our business likely will depend, in part, on our ability to acquire, in-license or use these intellectual property rights. In addition, with respect to any patent or other intellectual property rights that we co-own with third parties, we may require exclusive licenses to such co-owners' interest in such patent or other intellectual property rights. However, we may be unable to secure such licenses or otherwise acquire or in-license any intellectual property rights related to compositions, methods of use, processes or other components from third parties that we identify as necessary for our product candidates and our technology on commercially reasonable terms, or at all. Even if we are able to in-license any such necessary intellectual property, it could be on non-exclusive terms, thereby giving our competitors and other third parties access to the same intellectual property licensed to us, and the applicable licensors could require us to make substantial licensing and royalty payments. The licensing or acquisition of third-party intellectual property rights is a competitive area, and several more established companies may pursue strategies to license or acquire third-party intellectual property rights that we may consider attractive or necessary. These established companies may have a competitive advantage over us due to their size, capital resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment.

We sometimes collaborate with non-profit and 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 collaboration. Regardless of such option, we may be unable to negotiate a license within the specified timeframe or under terms that are acceptable to us. If we are unable to do so, the institution may offer the intellectual property rights to third parties, potentially blocking our ability to pursue our research program and develop and commercialize our product candidates.

If we are unable to successfully obtain rights to required third-party intellectual property rights or maintain the existing intellectual property rights we have licensed, we may be required to expend significant time and resources to redesign our product candidates or the methods for manufacturing them or to develop or license replacement technology, all of which may not be feasible

on a technical or commercial basis. If we are unable to do so, we may be unable to develop or commercialize the affected product candidates, which could have a material adverse effect on our business, financial condition, results of operations and prospects.

Issued patents covering our product candidates could be found invalid or unenforceable if challenged in court or before administrative bodies in the U.S. or abroad.

Our owned and licensed patent rights may be subject to priority, validity, inventorship and enforceability disputes. If we or our licensors are unsuccessful in any of these proceedings, such patent rights may be narrowed, invalidated or held unenforceable, we may be required to obtain licenses from third parties, which may not be available on commercially reasonable terms or at all, or we may be required to cease the development, manufacture and commercialization of one or more of our product candidates. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

If we or one of our licensors initiate legal proceedings against a third party to enforce a patent covering our product candidates or our technology, the defendant could counterclaim that the patent covering the product candidate or technology is invalid or unenforceable. In patent litigation in the U.S., defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, lack of written description or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld information material to patentability from the USPTO, or made a misleading statement, during prosecution. Third parties also may raise similar claims before administrative bodies in the U.S. or abroad, even outside the context of litigation. Such mechanisms include re-examination, interference proceedings, derivation proceedings, post grant review, inter partes review and equivalent proceedings such as opposition, invalidation and revocation proceedings in foreign jurisdictions. Such proceedings could result in the revocation or cancellation of or amendment to our patents in such a way that they no longer cover our product candidates or our technology or prevent third parties from competing with our product candidates or our technology. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which the patent examiner and we or our licensing partners were unaware during prosecution. If a third party were to prevail on a legal assertion of invalidity or unenforceability, we could lose at least part, and perhaps all, of the patent protection on one or more of our product candidates or technology. Such a loss of patent protection could have a material adverse effect on our business, financial condition, results of operations and prospects.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

In addition to the protection afforded by patents, we rely on trade secret protection and confidentiality agreements to protect proprietary know-how that is not patentable or that we elect not to patent, processes for which patents are difficult to enforce and any other elements of our product candidate discovery and development processes that involve proprietary know-how, information or technology that is not covered by patents. However, trade secrets can be difficult to protect and some courts inside and outside the U.S. are less willing or unwilling to protect trade secrets. We seek to protect our proprietary technology and processes, in part, by entering into confidentiality agreements with our employees, consultants, scientific advisors, contractors and other parties who have access to such technology and processes. However, we may not be able to prevent the unauthorized disclosure or use of our technical know-how or other trade secrets by the parties to these agreements. Monitoring unauthorized uses and disclosures is difficult, and we do not know whether the steps we have taken to protect our proprietary technologies will be effective. If any of the collaborators, scientific advisors, employees and consultants who are parties to these agreements breach or violate the terms of any of these agreements, we may not have adequate remedies for any such breach or violation. As a result, we could lose our trade secrets and third parties could use our trade secrets to compete with our product candidates and our technology. Additionally, we cannot guarantee that we have entered into such agreements with each party that may have or has had access to our trade secrets or proprietary technology and processes.

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; however, such systems and security measures may be breached, and we may not have adequate remedies for any breach.

In addition, our trade secrets may otherwise become known or be independently discovered by competitors or other third parties. Competitors or third parties could purchase our product candidates or our technology and attempt to replicate some or all of the competitive advantages we derive from our development efforts, willfully infringe our intellectual property rights, design around our intellectual property rights or develop their own competitive technologies that fall outside the scope of our intellectual property rights. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor or other third party, we would have no right to prevent them, or those to whom they communicate such trade secrets, from using that technology or information to compete with us. If our trade secrets are not adequately protected so as to protect our market against competitors' products, our business, financial condition, results of operations and prospects could be materially and adversely affected.

Third parties may initiate legal proceedings alleging that we are infringing, misappropriating or otherwise violating their intellectual property rights, the outcome of which would be uncertain and could harm our business.

Our commercial success depends upon our ability and the ability of our collaborators, if any, to develop, manufacture, market and sell our product candidates and use our proprietary technologies without infringing, misappropriating or otherwise violating the intellectual property rights of third parties. The biotechnology and pharmaceutical industries are characterized by extensive and complex litigation regarding patents and other intellectual property rights. We may become party to, or be threatened with, adversarial proceedings or litigation in which third parties may assert infringement, misappropriation or other violation claims against us, alleging that our product candidates, manufacturing methods, formulations or administration methods are covered by their patents. Given the vast number of patents and other intellectual property in our field of technology, we cannot be certain or guarantee that we do not infringe, misappropriate or otherwise violate patents or other intellectual property. Other companies and institutions have filed, and continue to file, patent applications that may be related to our technology and, more broadly, to gene therapy and related manufacturing methods. Some of these patent applications have already been allowed or issued and others may issue in the future. Since this area is competitive and of strong interest to pharmaceutical and biotechnology companies, there will likely be additional patent applications filed and additional patents granted in the future, as well as additional research and development programs expected in the future. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are pursuing development candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that we may be subject to claims of infringement of the patent rights of third parties. If a patent holder believes the manufacture, use, sale or importation of our product candidates or our technology infringes its patent, the patent holder may sue us even if we have licensed other patent rights for our technology.

We are aware of certain patents in the U.S. and other jurisdictions owned by third parties that claim subject matter that relates to our product candidates and the EDO platform. Such third parties may assert these patents against us in litigation in the U.S. or other jurisdictions. The outcome of any such litigation is uncertain and, even if we prevail, the costs of such litigation could have a material adverse effect on our financial position, result in disclosure of our trade secrets, distract key personnel from the continued development of our business, and adversely affect our ability to enter or maintain commercial relationships with collaborators, clients or customers. If we are unsuccessful in such litigation, we could be prevented from commercializing products or could be required to take licenses from such third parties which may not be available on commercially reasonable terms, if at all.

It is also possible that we have failed to identify relevant third-party patents or applications. Because patent applications can take many years to issue, may be confidential for 18 months or more after filing and can be revised before issuance, there may be applications now pending which may later result in issued patents that may be infringed by the manufacture, use, sale or importation of our product candidates or our technology and we may not be aware of such patents. Furthermore, applications filed before November 29, 2000 and certain applications filed after that date that will not be filed outside the U.S. may remain confidential until a patent issues. Moreover, it is difficult for industry participants, including us, to identify all third-party patent rights that may be relevant to our product candidates and our technologies because patent searching is imperfect due to differences in terminology among patents, incomplete databases and the difficulty in assessing the meaning of patent claims. We may fail to identify relevant patents or patent applications or may identify pending patent applications of potential interest but incorrectly predict the likelihood that such patent applications may issue with claims of relevance to our technology. In addition, we may incorrectly conclude that a third-party patent is invalid, unenforceable or not infringed by our activities. Additionally, pending patent applications that have been published can, subject to certain limitations, be later amended in a manner that could cover our technologies, our product candidates or the use of our product candidates.

Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future, regardless of their merit. There is a risk that third parties may choose to engage in litigation with us to enforce or to otherwise assert their patent rights against us. Even if we believe such claims are without merit, a court of competent jurisdiction could hold that these third-party patents are valid, enforceable and infringed, which could adversely affect our ability to commercialize our product candidates or technologies covered by the asserted third-party patents. In order to successfully challenge the validity of any such U.S. patent in federal court, we would need to overcome a presumption of validity. As this burden is a high one requiring us to present clear and convincing evidence as to the invalidity of any such U.S. patent claim, there is no assurance that a court of competent jurisdiction would invalidate the claims of any such U.S. patent. If we are found to infringe a third party's valid and enforceable intellectual property rights, we could be required to obtain a license from such third party to continue developing, manufacturing and marketing our product candidates and our technology. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors and other third parties access to the same technologies licensed to us, and it could require us to make substantial licensing and royalty payments. We could be forced, including by court order, to cease developing, manufacturing and commercializing the infringing technology or product candidates. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees, if we are found to have willfully infringed a patent or other intellectual property right. A finding of infringement could prevent us from manufacturing and commercializing our product candidates or force us to cease some of our business operations, which could harm our business. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business, financial condition, results of operations and prospects.

Intellectual property litigation or other proceedings could cause us to spend substantial resources and distract our personnel from their normal responsibilities.

Competitors may challenge the validity and enforceability of our patent rights or those of our licensing partners, infringe, misappropriate or otherwise violate our or our licensors' patent and other intellectual property rights, or we may be required to defend against claims of infringement, misappropriation or other violation. Litigation and other proceedings in connection with any of the foregoing claims can be unpredictable, expensive and time-consuming. Even if resolved in our favor, litigation or other proceedings relating to intellectual property claims may cause us to incur significant expenses and could distract our scientific, technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities.

We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors or other third parties may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and more mature and developed intellectual property portfolios. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could adversely affect our ability to compete in the marketplace and could have a material adverse effect on our business, financial condition, results of operations and prospects.

We may be subject to claims asserting that our employees, consultants or advisors have wrongfully used or disclosed alleged trade secrets of their current or former employers or claims asserting ownership of what we regard as our own intellectual property.

Many of our employees, consultants or advisors are currently, or were previously, employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees, consultants and advisors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that these individuals or we have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such individual's current or former employer. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or be required to obtain licenses to such intellectual property rights, which may not be available on commercially reasonable terms or at all. An inability to incorporate such intellectual property rights would harm our business and may prevent us from successfully commercializing our product candidates. In addition, we may lose personnel as a result of such claims and any such litigation, or the threat thereof may adversely affect our ability to hire employees or contract with independent contractors. A loss of key personnel or their work product could hamper or prevent our ability to commercialize our product candidates and our technology, which would have a material adverse effect on our business, results of operations, financial condition and prospects. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to our scientific and management personnel.

In addition, while it is our policy to require our employees and contractors who may be involved in the conception or development of intellectual property to execute agreements assigning such intellectual property to us, 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. Moreover, even when we obtain agreements assigning intellectual property to us, the assignment of intellectual property rights may not be self-executing or the assignment agreements may be breached, and we may be forced to bring claims against third parties, or defend claims that they may bring against us, to determine the ownership of what we regard as our intellectual property. Furthermore, individuals executing agreements with us may have pre-existing or competing obligations to a third party, such as an academic institution, and thus an agreement with us may be ineffective in perfecting ownership of inventions developed by that individual. Disputes about the ownership of intellectual property that we own may have a material adverse effect on our business, financial condition, results of operations and prospects.

In addition, we or our licensors may in the future be subject to claims by former employees, consultants or other third parties asserting an ownership right in our owned or licensed patent rights. An adverse determination in any such submission or proceeding 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 technology and therapeutics, without payment to us, or could limit the duration of the patent protection covering our technology and our product candidates. Such challenges may also result in our inability to develop, manufacture or commercialize our technology and product candidates without infringing third-party patent rights. In addition, if the breadth or strength of protection provided by our owned or licensed patent rights are threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future technology and product candidates. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

If we do not obtain patent term extension for our product candidates, our business may be harmed.

Under the Hatch-Waxman Amendments to the FDCA, a company may file an ANDA seeking approval of a generic version of an approved innovator product. Depending upon the timing, duration and specifics of any FDA marketing approval of our product candidates and our technology, one or more of our U.S. patents that we license or may own in the future may be eligible for limited patent term extension under Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent extension term of up to five years as compensation for patent term lost during the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent may be extended and only those claims covering the approved product, a method for using it or a method for manufacturing it may be extended. The application for the extension must be submitted prior to the expiration of the patent for which extension is sought. A patent that covers multiple products for which approval is sought can only be extended in connection with one of the approvals. However, we may not be granted an extension because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. In addition, to the extent we wish to pursue patent term extension based on a patent that we in-license from a third party, we would need the cooperation of that third party. If we are unable to obtain patent term extension or the term of any such extension is less than we request, our competitors may obtain approval of competing products following our patent expiration, and our revenue could be reduced. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

We may be subject to claims challenging the inventorship or ownership of our patent and other intellectual property rights.

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 patent rights, trade secrets or other intellectual property as an inventor or co-inventor. For example, we or our licensors may have inventorship disputes arise from conflicting obligations of employees, consultants or others who are involved in developing our product candidates or technology. Litigation may be necessary to defend against these and other claims challenging inventorship or our or our licensors' ownership of our owned or in-licensed patent rights, trade secrets or other intellectual property. If we or our licensors fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of or right to use intellectual property that is important to our product candidates or our technology. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected.

Our current and future trademark applications in the U.S. and other foreign jurisdictions may not be allowed or may be subsequently opposed. Once filed and registered, our trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. As a means to enforce our trademark rights and prevent infringement, we may be required to file trademark claims against third parties or initiate trademark opposition proceedings. This can be expensive and time-consuming, particularly for a company of our size. We may not be able to protect our rights to these trademarks and trade names, which we need to build name recognition among potential partners or customers in our markets of interest. At times, third parties 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 registered or unregistered trademarks or trade names. Over the long term, if we are unable to establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively and our business may be adversely affected. Our efforts to enforce or protect our proprietary rights related to trademarks, trade secrets, domain names, copyrights or other intellectual property may be ineffective and could result in substantial costs and diversion of resources. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations or prospects.

Intellectual property rights do not necessarily address all potential threats.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations and may not adequately protect our business or permit us to maintain our competitive advantage. For example:

- others may be able to make products that are similar to our product candidates but that are not covered by intellectual property, including the claims of the patents, that we own or license currently or in the future;

- we, or our license partners or current or future collaborators, might not have been the first to make the inventions covered by the issued patent or pending patent application that we own or license currently or in the future;
- we, or our license partners or current or future collaborators, might not have been the first to file patent applications covering certain of our or their inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing, misappropriating, or otherwise violating our owned or licensed intellectual property rights;
- it is possible that our or our licensors' current or future pending patent applications will not lead to issued patents;
- issued patents that we hold rights to may be held invalid or unenforceable, including as a result of legal challenges by third parties;
- third parties might conduct research and development activities in jurisdictions where we do not have patent or other intellectual property rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we may not develop additional proprietary technologies that are patentable;
- the patents or other intellectual property rights of others may have an adverse effect on our business; and
- we may choose not to file a patent for certain trade secrets or know-how, and a third party may subsequently file a patent covering such intellectual property.

Should any of these events occur, they could significantly harm our business, financial condition, results of operations and prospects.

Our reliance on third parties requires us to share our trade secrets, which increases the possibility that a competitor or other third party will discover our trade secrets or that our trade secrets will be misappropriated or disclosed.

Because we currently rely on certain third parties to manufacture all or part of our product candidates and to perform quality testing, and because we may need to collaborate with various third parties for the advancement of our product candidates and technology, we may be required to, at times, share our proprietary technology and confidential information, including trade secrets, with them. We seek to protect our proprietary technology, in part, by entering into confidentiality agreements and, if applicable, material transfer agreements, collaboration agreements, services agreements, consulting agreements and other similar agreements prior to beginning research or disclosing any proprietary information to such third parties. These agreements typically limit the rights of the third parties to use or disclose our confidential information, including our trade secrets. Despite the contractual provisions employed when working with third parties, the need to share trade secrets and other confidential information increases the risk that such trade secrets become known by our competitors or other third parties, are inadvertently incorporated into the technology of others or are disclosed or used in violation of these agreements. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time consuming, and the outcome is unpredictable. In addition, some courts inside and outside the U.S. are less willing or unwilling to protect trade secrets. We may need to share our proprietary information, including trade secrets, with future business partners, collaborators, contractors and others located in countries at heightened risk of theft of trade secrets, including through direct intrusion by private parties or foreign actors, and those affiliated with or controlled by state actors. Further, if any of our trade secrets were to be lawfully obtained or independently developed by a competitor or other third-party, we would have no right to prevent them from using that technology or information to compete with us. Despite our efforts to protect our trade secrets, our competitors may discover our trade secrets, either through breach of these agreements, independent development or publication of information including our trade secrets by third parties. Given that our proprietary position is based, in part, on our know-how and trade secrets, a competitor's or other third party's discovery of our proprietary technology and confidential information or other unauthorized use or disclosure would impair our competitive position and may harm our business, financial condition, results of operations and prospects.

Risks Related to Employee Matters, Managing Growth and Other Operational Matters

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

We are highly dependent on the research and development, clinical, financial, operational and other business expertise of our executive officers, as well as the other principal members of our management, scientific and clinical teams. Although we have entered into employment agreements with our executive officers, each of them may terminate their employment with us at any time. We do not maintain "key person" insurance for any of our executives or other employees. Recruiting and retaining qualified scientific, clinical, manufacturing, accounting, legal and sales and marketing personnel will also be critical to our success.

The loss of the services of our executive officers or other key employees could impede the achievement of our research, development and commercialization objectives and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval of and commercialize products. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. Our success as a public company also depends on implementing and maintaining internal controls and the accuracy and timeliness of our financial reporting. If we are unable to continue to attract and retain high quality personnel, our ability to pursue our growth strategy will be limited.

We expect to expand our headcount to support our development and regulatory capabilities and potentially implement sales, marketing and distribution capabilities, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.

As of December 31, 2024, we had 81 full-time employees. As our development progresses, we expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of drug development, clinical, regulatory affairs and, if any product candidate receives marketing approval, sales, marketing, distribution and coverage and reimbursement capabilities. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, and continue to recruit and train additional qualified personnel and may need to expand our facilities. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. The expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

As a growing biotechnology company, we expect to pursue new platforms and product candidates in several therapeutic areas and across a range of diseases. Successfully developing product candidates for, and fully understanding the regulatory and manufacturing pathways to, each of these therapeutic areas and disease states requires a significant depth of talent, resources and corporate processes in order to allow simultaneous execution across multiple areas. Due to our limited resources, we may not be able to effectively manage this simultaneous execution and the expansion of our operations or recruit and train additional qualified personnel. This may result in weaknesses in our infrastructure, give rise to operational mistakes, legal or regulatory compliance failures, loss of business opportunities, loss of employees and reduced productivity among remaining employees. The physical expansion of our operations may lead to significant costs and may divert financial resources from other projects, such as the development of our product candidates. If our management is unable to effectively manage our expected development and expansion, our expenses may increase more than expected, our ability to generate or increase our revenue could be reduced and we may not be able to implement our business strategy. Our future financial performance and our ability to compete effectively and commercialize our product candidates, if approved, will depend in part on our ability to effectively manage the future development and expansion of our company.

Our international activities subject us to various risks, and our failure to manage these risks could adversely affect our results of operations.

We face significant operational risks as a result of doing business internationally, such as:

- fluctuations in foreign currency exchange rates;
- differing payor reimbursement regimes, governmental payors or patient self-pay systems and price controls;
- potentially adverse and/or unexpected tax consequences, including penalties due to the challenge by tax authorities on our tax position;
- potential changes to the accounting standards, which may influence our financial situation and results;
- compliance with tax, employment, immigration and labor laws should we have any employees living or traveling abroad;
- becoming subject to the different, complex and changing laws, regulations and court systems of multiple jurisdictions and compliance with a wide variety of foreign laws, treaties;

- reduced protection of, or significant difficulties in enforcing, intellectual property rights, or increased risk of intellectual property disputes, in certain countries;
- difficulties in attracting and retaining qualified consultants, contractors, and personnel;
- restrictions imposed by any applicable local labor practices and laws on our business and operations, including unilateral cancellation or modification of contracts;
- rapid changes in global government, economic and political policies and conditions, political or civil unrest or instability, terrorism or epidemics and other similar outbreaks or events, and potential failure in confidence of our suppliers or customers due to such changes or events;
- geopolitical tensions that affect our activities, operations and/or operations of our contractors, consultants, collaborators, vendors or partners; and
- tariffs, trade protection measures, import or export licensing requirements, trade embargoes and other trade barriers.

Future acquisitions or strategic alliances could disrupt our business and harm our financial condition and results of operations.

We may acquire additional businesses, technologies or assets, form strategic alliances or create joint ventures with third parties that we believe will complement or augment our existing business. If we acquire businesses with promising markets or technologies, we may not be able to realize the benefit of acquiring such businesses if we are unable to successfully integrate them with our existing operations and company culture. We may encounter numerous difficulties in developing, manufacturing and marketing any new products or product candidates resulting from a strategic alliance or acquisition that delay or prevent us from realizing their expected benefits or enhancing our business. We cannot assure you that, following any such acquisition, we will achieve the expected synergies to justify the transaction. The risks we face in connection with acquisitions, include:

- diversion of management time and focus from operating our business to addressing acquisition integration challenges;
- coordination of research and development efforts;
- retention of key employees from the acquired company;
- changes in relationships with collaborators as a result of product acquisitions or strategic positioning resulting from the acquisition;
- cultural challenges associated with integrating employees from the acquired company into our organization;
- the need to implement or improve controls, procedures and policies at a business that prior to the acquisition may have lacked sufficiently effective controls, procedures and policies;
- liability for activities of the acquired company before the acquisition, including intellectual property infringement claims, violation of laws, commercial disputes, tax liabilities and other known liabilities;
- unanticipated write-offs or charges; and
- litigation or other claims in connection with the acquired company, including claims from terminated employees, customers, former stockholders or other third parties.

Our failure to address these risks or other problems encountered in connection with our past or future acquisitions or strategic alliances could cause us to fail to realize the anticipated benefits of these transactions, cause us to incur unanticipated liabilities and harm the business generally. There is also a risk that future acquisitions will result in the incurrence of debt, contingent liabilities, amortization expenses or incremental operating expenses, any of which could harm our financial condition or results of operations.

Our internal information technology systems, or those of our vendors, collaborators or other contractors or consultants, may fail or suffer from cyber security incidents or breaches, loss or leakage of data and other disruptions or compromise, which could result in a material disruption of our product development programs, compromise sensitive information related to our business or prevent us from accessing critical information, or trigger contractual and legal obligations, potentially exposing us to liability, reputational harm or otherwise adversely affecting our business and financial results.

We are increasingly dependent upon information technology systems and infrastructure to operate our business. In the ordinary course of business, we collect, store and transmit confidential information (including but not limited to intellectual property, proprietary business information and personal information). It is critical that we, our vendors, collaborators and other contractors or consultants, do so in a secure manner to maintain the availability, security, confidentiality, privacy and integrity of such confidential information.

Despite the implementation of security measures, given the size and complexity of our internal information technology systems and those of our current and future vendors, collaborators and other contractors or consultants, and the increasing amounts of confidential information that we and our affiliated third parties maintain, such information technology systems are still vulnerable to damage or interruption from computer viruses, computer hackers, malicious code, ransomware, social engineering attacks (including phishing attacks), employee error, theft or misuse, denial-of-service attacks, sophisticated nation-state and nation-state-supported actors, unauthorized access, natural disasters, terrorism, war, telecommunication and electrical failures or other compromise. The risk of a cybersecurity incident, breach or disruption, particularly through cyber-attacks or cyber intrusion, including by computer hackers, foreign governments and cyber terrorists, has generally increased as the number, intensity and sophistication of attempted attacks and intrusions from around the world have increased. As a result of the effects of a pandemic, such as the COVID-19 pandemic or other health crisis, we may also face increased cybersecurity risks due to our reliance on internet technology and the number of our employees who are working remotely for a portion of their time, which may create additional opportunities for cybercriminals to exploit vulnerabilities. The techniques used by cyber criminals change frequently, may not be recognized until launched, and can originate from a wide variety of sources, including outside groups such as external service providers, organized crime affiliates, terrorist organizations or hostile foreign governments or agencies. As such, we may experience cybersecurity incidents, breaches, or compromises that may remain undetected for an extended period. We may be unable to anticipate all types of cybersecurity threats, or implement preventive measures effective against all such cybersecurity threats. 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 and certain of our service providers are from time to time subject to cyberattacks and cybersecurity incidents, breaches, or compromises. While we do not believe that we have experienced any significant system failure, accident or cybersecurity breach or incident to date, if such an event were to occur, it could result in a disruption of our development programs and our business operations, whether due to a loss of our trade secrets or other proprietary or confidential information or other disruptions. For example, the loss of clinical trial data from clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. If we were to experience a significant cybersecurity incident or breach of our information systems or data, the costs associated with the investigation, remediation and potential notification of the incident or breach to counterparties, data subjects, regulators or others could be material. In addition, our remediation efforts may not be successful. Moreover, if the information technology systems of our vendors, collaborators and other contractors and consultants become subject to disruptions or cybersecurity incidents or breaches, we may have insufficient recourse against such third parties and we may have to expend significant resources to mitigate the impact of such an event, and to develop and implement protections to prevent future events of this nature from occurring. If we do not allocate and effectively manage the resources necessary to build and sustain the proper technology and cybersecurity infrastructure, we could suffer significant business disruption, including transaction errors, supply chain or manufacturing interruptions, processing inefficiencies, data loss or the loss of or damage to intellectual property or other proprietary information.

To the extent that any disruption, cybersecurity incident, breach, or compromise were to result in a loss of, or damage to, our or our vendors', collaborators' or other contractors' or consultants' data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability, including litigation exposure and penalties and fines. Any such event that leads to unauthorized access, use, or disclosure of personal information, including personal information regarding our customers or employees, could harm our reputation, compel us to comply with federal and/or state breach notification laws and foreign law equivalents, subject us to mandatory corrective action, and otherwise subject us to liability under laws and regulations that protect the privacy and security of personal information. We could become the subject of regulatory action or investigation, and our competitive position and reputation could be harmed and the further development and commercialization of our product candidates could be delayed. As a result of such an event, we may also be in breach of our contractual obligations. Any of the above could have a material adverse effect on our business, financial condition, results of operations or prospects.

The financial exposure from the events referenced above could either not be insured against or not be fully covered through any insurance that we maintain. In addition, we cannot be sure that our existing insurance coverage will continue to be available on acceptable terms or that our insurers will not deny coverage as to any future claim. There can be no assurance that the limitations of liability in our contracts would be enforceable or adequate or would otherwise protect us from liabilities or damages as a result of the events referenced above.

Our operations or those of the third parties upon whom we depend might be affected by the occurrence of a natural disaster, pandemic or other catastrophic event.

We depend on our employees, consultants, CDMOs and CROs, as well as regulatory agencies and other parties, for the continued operation of our business. While we maintain disaster recovery plans, they might not adequately protect us. Despite any precautions we take for natural disasters or other catastrophic events, these events, including terrorist attack, pandemics, hurricanes, fire, floods and ice and snowstorms, could result in significant disruptions to our research and development, preclinical studies, clinical trials, and, ultimately, commercialization of our products. Long-term disruptions in the infrastructure caused by events, such

as natural disasters, the outbreak of war, the escalation of hostilities and acts of terrorism or other “acts of God,” particularly involving cities in which we have offices, manufacturing or clinical trial sites, could adversely affect our businesses. Although we carry business interruption insurance policies and typically have provisions in our contracts that protect us in certain events, our coverage might not respond or be adequate to compensate us for all losses that may occur. Any natural disaster or catastrophic event affecting us, our CDMOs, CROs, regulatory agencies or other parties with which we are engaged could have a significant negative impact on our operations and financial performance.

Adverse developments affecting the financial services industry, such as actual events or concerns involving liquidity, defaults, or non-performance by financial institutions or transactional counterparties, could adversely affect our current and projected business operations and our financial condition and results of operations.

Events involving limited liquidity, defaults, non-performance or other adverse developments that affect financial institutions, transactional counterparties or other companies in the financial services industry or the financial services industry generally, or concerns or rumors about any events of these kinds or other similar risks, have in the past and may in the future lead to market-wide liquidity problems. Although we are not a borrower or party to any such instruments with any financial institution that has experienced such events, if we were to borrow money in the future and if any of our lenders or counterparties to any such instruments were to be placed into receivership, we may be unable to access such funds. In addition, if any of our customers, suppliers or other parties with whom we conduct business are unable to access funds pursuant to such instruments or lending arrangements with such a financial institution, such parties’ ability to pay or perform their obligations to us or to enter into new commercial arrangements requiring additional payments to us or additional funding could be adversely affected. In this regard, counterparties to credit agreements and arrangements with banks in receivership or other financial difficulty, and third parties such as beneficiaries of letters of credit (among others), may experience direct impacts from the closure or reorganization of such financial institutions and uncertainty remains over liquidity concerns in the broader financial services industry. Similar impacts have occurred in the past, such as during the 2008-2010 financial crisis.

Inflation and rapid increases in interest rates have led to a decline in the trading value of previously issued government securities with interest rates below current market interest rates. Although the U.S. Department of Treasury, FDIC and Federal Reserve Board have announced a program to provide up to \$25 billion of loans to financial institutions secured by certain government securities held by financial institutions to mitigate the risk of potential losses on the sale of such instruments, widespread demands for customer withdrawals or other liquidity needs of financial institutions for immediate liquidity may exceed the capacity of such program. Additionally, there is no guarantee that the U.S. Department of Treasury, FDIC and Federal Reserve Board will provide access to uninsured funds in the future in the event of the closure of other banks or financial institutions in the future, or that they would do so in a timely fashion.

Although we assess our banking relationships as we believe necessary or appropriate, our access to funding sources in amounts adequate to finance or capitalize our current and projected future business operations could be significantly impaired by factors that affect us, the financial institutions with which we have financial arrangements directly, or the financial services industry or economy in general. These factors could include, among others, events such as liquidity constraints or failures, the ability to perform obligations under various types of financial, credit or liquidity agreements or arrangements, disruptions or instability in the financial services industry or financial markets, or concerns or negative expectations about the prospects for companies in the financial services industry.

In addition, investor concerns regarding the U.S. or international financial systems could result in less favorable commercial financing terms, including higher interest rates or costs and tighter financial and operating covenants, or systemic limitations on access to credit and liquidity sources, thereby making it more difficult for us to acquire financing on acceptable terms or at all. Any decline in available funding or access to our cash and liquidity resources could, among other risks, adversely impact our ability to meet our operating expenses, financial obligations or fulfill our other obligations, result in breaches of our financial and/or contractual obligations or result in violations of federal or state wage and hour laws. Any of these impacts, or any other impacts resulting from the factors described above or other related or similar factors not described above, could have material adverse impacts on our liquidity, our current and/or projected business operations, and financial condition and results of operations.

The effects of the COVID-19 pandemic, or a future pandemic, epidemic or outbreak of an infectious or highly contagious disease, may materially and adversely affect our business and financial results and could cause a disruption in the development of our product candidates.

Public health crises such as pandemics, including the COVID-19 pandemic or similar outbreaks, could adversely impact our business. For example, in connection with COVID-19, we and our CDMOs and CROs have in the past experienced a reduction in the capacity to undertake research-scale production and to execute some preclinical studies, and we may face future similar disruptions that affect our ability to initiate and complete preclinical studies. We may also encounter disruptions in procuring items that are essential for our research and development activities, such as raw materials used in the manufacture of any product candidates,

laboratory supplies used in our preclinical and clinical studies, or animals that are used for preclinical testing for which there are or may be shortages because of ongoing efforts to address COVID-19 or a future health pandemic. The ultimate extent to which COVID-19, or a future outbreak of other highly infectious or contagious diseases, impacts our operations or those of our third-party partners, including our preclinical studies or clinical trial operations, will depend on future developments, which are highly uncertain and cannot be predicted with confidence, including the scope, severity and duration of an outbreak, actions taken to contain an outbreak or mitigate its impact, and the direct and indirect economic effects of an outbreak and containment measures, among other developments.

Risks Related to Ownership of Our Common Stock

The stock price of our common stock has been and may continue to be volatile or may decline regardless of our operating performance and prospects.

You may not be able to sell your shares quickly or at the market price if trading in shares of our common stock is not active. An active or liquid market in our common stock may not develop or, if it does develop, it may not be sustainable, and the prices at which shares of our common stock trade in the market have fluctuated considerably and may fluctuate in the future considerably or decline or be quite volatile regardless of our operating performance and prospects. As a result of these and other factors, you may be unable to resell your shares of our common stock at or above the initial public offering price or the per share price you paid for your shares. Further, an inactive market may also impair our ability to raise capital by selling shares of our common stock and may impair our ability to enter into strategic collaborations or acquire companies or products by using our shares of common stock as consideration.

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 offerings, debt financings, collaborations, strategic alliances and/or licensing arrangements. We do not have any committed external source of funds. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a common stockholder. In February 2024, we sold shares of our common stock under our ATM program and in the Follow-on Offering, receiving aggregate net proceeds of \$86.3 million after deducting underwriters' fees and costs of the offerings. Any debt financing or 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, selling or licensing our assets, making capital expenditures, declaring dividends or encumbering our assets to secure future indebtedness.

If we raise additional funds through collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, 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 or other arrangements when needed or on terms acceptable to us, we may be required to delay, limit, reduce or eliminate some or all of our research and development programs, pipeline expansion or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

If securities or industry analysts do not continue to publish research or reports or publish inaccurate or unfavorable research or reports about our business, our stock price and trading volume could decline.

The trading market for our common stock depends in part on the research and reports that securities or industry analysts publish about us or our business. We do not have any control over these analysts. In the event one or more analysts downgrade our stock price or change their opinion of our stock price, our stock price would likely decline. In addition, if one or more analysts cease coverage of our company or fail to regularly publish reports on us, we could lose visibility in the financial markets, which could cause our stock price or trading volume to decline.

The price of our common stock is volatile and fluctuates substantially, which could result in substantial losses for holders of our common stock.

The stock market in general, and the market for smaller biopharmaceutical companies in particular, have experienced extreme price volatility and volume fluctuations that have often been unrelated to the operating performance of particular companies. As a result of this volatility, you may not be able to sell your common stock at or above the price you paid for it. The market price for our common stock may be influenced by many factors, including:

- timing and results of, or developments in, preclinical studies and clinical trials of our product candidates or those of our competitors or potential competitors;

- adverse regulatory rulemaking, guidance or decisions, including failure to receive marketing approvals for our product candidates;
- our success in commercializing any product candidates that may be approved;
- the success of competitive products or technologies;
- regulatory or legal developments in the U.S. and other countries;
- developments or disputes concerning patent applications, issued patents or other intellectual property or proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to our product candidates;
- the results of our efforts to discover, develop, acquire or in-license products, product candidates, technologies or data referencing rights, the costs of commercializing any such products and the costs of development of any such product candidates or technologies;
- actual or anticipated changes in estimates as to our financial condition or results, clinical outcomes, development timelines or recommendations by securities analysts;
- variations in our financial condition or results or the financial condition or results of companies that are perceived to be similar to us;
- sales of our common stock by us, our executive officers, directors or principal stockholders or others;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry, political and market conditions, including conditions resulting from the effects of the COVID-19 pandemic, high inflation and capital market disruptions, and government macroeconomic policies; and
- the other factors described in this “*Risk factors*” section.

Any of the factors listed above could materially adversely affect your investment in our common stock, and our common stock may trade at prices significantly below the price you paid for our stock, which could contribute to a loss of all or part of your investment. In such circumstances the trading price of our common stock may not recover and may experience a further decline. In the past, following periods of volatility in the market price of a company’s securities, securities class-action litigation has often been instituted against that company. Any lawsuit to which we are a party, with or without merit, may result in an unfavorable judgment. We also may decide to settle lawsuits on unfavorable terms. Any such negative outcome could result in payments of substantial damages or fines, damage to our reputation or adverse changes to our offerings or business practices. Such litigation may also cause us to incur other substantial costs to defend such claims and maintain liability insurance coverages and may also result in the diversion of management’s attention and resources.

Unfavorable global economic conditions could adversely affect our business, financial condition, stock price and results of operations.

Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets. For example, the 2008 global financial crisis caused extreme volatility and disruptions in the capital and credit markets. A severe or prolonged economic downturn resulting from the effects of the COVID-19 pandemic or future pandemic could result in a variety of risks to our business, including weakened demand for our product candidates and our ability to raise additional capital when needed on acceptable terms, if at all. In addition, the current military conflict between Russia and Ukraine, armed conflict in Israel and the Gaza Strip and military action in other parts of the Middle East could disrupt or otherwise adversely impact our operations and those of third parties upon which we rely. Related sanctions, import/export controls or other actions that have been or may be initiated by nations, including the U.S. or the EU, including previously pending legislative proposals in the U.S. relating to China and certain biotechnology companies of concern, or actions taken by Russia (e.g., potential cyberattacks, disruption of energy flows, etc.) could adversely affect our business and/or our supply chain, our CROs, CDMOs and other third parties with which we conduct business. A weak or declining economy could also strain our suppliers, possibly resulting in supply disruption. If the current equity and credit markets deteriorate, it may make any necessary debt or equity financing more difficult, more costly, and more dilutive. Failure to secure any necessary financing in a timely manner and on favorable terms could impair our ability to achieve our growth strategy, could harm our financial performance and stock price and could require us to delay or abandon clinical development plans. In addition, there is a risk that our current or future service providers, manufacturers or other collaborators may not survive such difficult economic times, which could directly affect our ability to attain our operating goals on schedule and on budget. We cannot anticipate

all of the ways in which the current economic climate, including increasing interest rates and high inflation, and financial market conditions could adversely impact our business.

Our executive officers, directors and principal shareholders, if they choose to act together, will continue to have the ability to significantly influence all matters submitted to stockholders for approval.

Based upon our common stock outstanding as of December 31, 2024, our executive officers, directors, greater than five percent shareholders and their affiliates beneficially own approximately 51.9% of our outstanding common stock. As a result, if these stockholders were to choose to act together, they would be able to significantly influence all matters submitted to our stockholders for approval, as well as our management and affairs, even though some of these persons or entities may have interests that are different than those of yours. For example, these stockholders, if they choose to act together, could significantly influence the election of directors and approval of any merger, consolidation or sale of substantially all of our assets. This concentration of ownership may:

- delay, defer or prevent a merger, consolidation or sale of all or substantially all of our assets that may be desired by other stockholders;
- delay, defer or prevent a change in control transaction involving us that other stockholders may desire; or
- entrench our management and board of directors.

Because we do not anticipate paying any cash dividends on our capital stock in the foreseeable future, capital appreciation, if any, will be your sole source of gain.

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. As a result, capital appreciation, if any, of our common stock will be your sole source of gain for the foreseeable future.

The sale of a significant number of shares of our common stock, or the perception that such sales could occur, could cause the market price of our common stock to drop significantly, even if our business is doing well.

Sales of a substantial number of shares of our common stock in the public market, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock, impair our ability to raise capital through the sale of additional equity securities, and make it more difficult for you to sell your common stock at a time and price that you deem appropriate.

In addition, holders of an aggregate of 8,778,170 shares of our common stock have rights, subject to specified conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. We have also filed or will file registration statements on Form S-8 to register all of the shares of common stock that we are able to issue under our equity compensation plans. Shares registered under these registration statements on Form S-8 can be freely sold in the public market upon issuance, subject to volume limitations applicable to affiliates, vesting arrangements, exercise of options and any contractual restrictions that may apply to such shares.

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

We are an “emerging growth company,” or EGC, as defined in the Jumpstart Our Business Startups Act of 2012, or JOBS Act. We may remain an EGC until the end of the year that is the fifth anniversary of the closing of our IPO, although if the market value of our common stock that is held by non-affiliates exceeds \$700.0 million as of any June 30 before that time or if we have annual gross revenues of \$1.235 billion or more in any fiscal year, we would cease to be an EGC as of December 31 of the applicable year. We also would cease to be an EGC if we issue more than \$1.0 billion of non-convertible debt over a three-year period. For so long as we remain an EGC, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not EGCs. These exemptions include:

- not being required to comply with the auditor attestation requirements in the assessment of our internal control over financial reporting;
- 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 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.

Even after we no longer qualify as an EGC, we may continue to qualify as a smaller reporting company, which would allow us to take advantage of many of the same exemptions from disclosure requirements, including reduced disclosure obligations regarding executive compensation. In addition, if we are a smaller reporting company with less than \$100 million in annual revenue, we would not be required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404. In reliance on these exemptions, we have taken advantage of reduced reporting obligations in this 10-K.

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 more volatile.

In addition, the JOBS Act permits an EGC to take advantage of an extended transition period to comply with new or revised accounting standards applicable to public companies until those standards would otherwise apply to private companies. We have elected to take advantage of such extended transition period, which means that when a standard is issued or revised and it has different application dates for public or private companies, we will adopt the new or revised standard at the time private companies adopt the new or revised standard and will do so until such time that we either irrevocably elect to “opt out” of such extended transition period or no longer qualify as an EGC. We may choose to early adopt any new or revised accounting standards whenever such early adoption is permitted for private companies.

We incur substantial costs as a result of operating as a public company, and our management is required to devote substantial time to compliance initiatives and corporate governance practices.

As a public company, and even more so after we are no longer an EGC or a smaller reporting company, we incur or will incur significant legal, accounting and other expenses. The Sarbanes-Oxley Act of 2002, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of the Nasdaq Global Select Market and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel devote and will need to continue to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations have increased and may continue to increase our legal and financial compliance costs, particularly as we hire additional financial and accounting employees to meet public company internal control and financial reporting requirements and have made and will make some activities more time-consuming and costly compared to when we were a private company. For example, we expect that these rules and regulations may make it more difficult and more expensive for us to obtain director and officer liability insurance, and we might be forced to accept reduced policy limits and coverage or incur substantially higher costs to obtain the same or similar coverage. The impact of these events could also make it more difficult for us to attract and retain qualified members of our board of directors.

We cannot predict or estimate the amount of additional costs we may incur as a public company or the timing of such costs. These rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices. We intend to invest resources to comply with evolving laws, regulations and standards, and this investment may result in increased general and administrative expenses and a diversion of management’s time and attention from revenue-generating activities to compliance activities. If notwithstanding our efforts to comply with new laws, regulations and standards, we fail to comply, regulatory authorities may initiate legal proceedings against us and our business may be harmed.

Pursuant to Section 404, we are required to furnish a report by our management on our internal control over financial reporting beginning with this 10-K. However, while we remain an EGC or a smaller reporting company with less than \$100 million in annual revenue, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404 within the prescribed period, we are engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, including through hiring additional financial and accounting personnel, engaging outside consultants and adopting a detailed work plan to assess and document the adequacy of internal control over financial reporting, continuing steps to improve control processes as appropriate, validating through testing that controls are functioning as documented and implementing a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that we will not be able to conclude, within the prescribed timeframe or at all, that our internal control over financial reporting is effective as required by Section 404. If we identify one or more material weaknesses in our internal control over financial reporting, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements, particularly if such material weakness results in the necessity of a restatement of our historical financial statements.

If we fail to maintain an effective system of internal control over financial reporting, we may not be able to accurately report our financial results or prevent fraud. As a result, stockholders could lose confidence in our financial and other public reporting, which would harm our business and the trading price of our common stock.

Effective internal control over financial reporting is necessary for us to provide reliable financial reports and, together with adequate disclosure controls and procedures, is designed to prevent fraud. Any failure to implement required new or improved controls, or difficulties encountered in their implementation, could cause us to fail to meet our reporting obligations. In addition, any testing by us conducted in connection with Section 404, or any subsequent testing by our independent registered public accounting firm, may reveal deficiencies in our internal control over financial reporting that are deemed to be material weaknesses or that may require prospective or retroactive changes to our financial statements or identify other areas for further attention or improvement. Inferior internal controls could also cause investors to lose confidence in our reported financial information, which could harm our business and have a negative effect on the trading price of our stock.

We are required to disclose changes made in our internal controls and procedures on a quarterly basis and our management is required to assess the effectiveness of these controls annually. However, for as long as we are an EGC under the JOBS Act or a smaller reporting company with less than \$100 million in annual revenue, our independent registered public accounting firm will not be required to attest to the effectiveness of our internal control over financial reporting pursuant to Section 404. We could be an EGC for up to five fiscal years after our IPO, which occurred on May 6, 2022. An independent assessment of the effectiveness of our internal control over financial reporting could detect problems that our management's assessment might not. Undetected material weaknesses in our internal control over financial reporting could lead to financial statement restatements and require us to incur the expense of remediation, which could have a negative effect on the trading price of our stock.

Anti-takeover provisions in our corporate charter documents and under Delaware law could make an acquisition of our company, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current directors and members of management.

Anti-takeover provisions in our third amended and restated certificate of incorporation and our second amended and 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:

- establish a classified board of directors such that only one of three classes of directors is elected each year;
- allow the authorized number of our directors to be changed only by resolution of our board of directors;
- limit the manner in which stockholders can remove directors from our board of directors;
- establish advance notice requirements for stockholder proposals that can be acted on at stockholder meetings and nominations to our board of directors;
- require that stockholder actions must be effected at a duly called stockholder meeting and prohibit actions by our stockholders by written consent;
- limit who may call stockholder meetings;
- authorize our board of directors to issue preferred stock without stockholder approval, which could be used to institute a "poison pill" that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our board of directors; and
- require the approval of the holders of at least 66.7% of the votes that all our stockholders would be entitled to cast to amend or repeal specified provisions of our certificate of incorporation or bylaws.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, or DGCL, 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 second amended and restated bylaws designate the Court of Chancery of the State of Delaware and the federal district courts of the United States of America as the sole and exclusive forum for certain types of actions and proceedings that may be initiated by our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers and employees.

Our second amended and restated bylaws provide that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware (or, if the Court of Chancery of the State of Delaware does not have jurisdiction, the federal district court for the District of Delaware) will be the sole and exclusive forum for the following types of actions or proceedings under Delaware statutory or common law:

- any derivative action or proceeding brought on our behalf;
- any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers, employees or stockholders to our company or our stockholders;
- any action asserting a claim arising pursuant to any provision of the DGCL or as to which the DGCL confers jurisdiction on the Court of Chancery of the State of Delaware; or
- any action asserting a claim arising pursuant to any provision of our certificate of incorporation or bylaws (in each case, as they may be amended from time to time) or governed by the internal affairs doctrine.

These choice of forum provisions will not apply to suits brought to enforce a duty or liability created by the Exchange Act. Furthermore, Section 22 of the Securities Act, creates concurrent jurisdiction for federal and state courts over all such Securities Act actions. Accordingly, both state and federal courts have jurisdiction to entertain such claims. To prevent having to litigate claims in multiple jurisdictions and the threat of inconsistent or contrary rulings by different courts, among other considerations, our second amended and restated bylaws provide that, unless we consent in writing to the selection of an alternative forum, the federal district courts of the United States of America shall, to the fullest extent permitted by law, be the sole and exclusive forum for the resolution of any claims arising under the Securities Act. While the Delaware courts have determined that such choice of forum provisions are facially valid, a stockholder may nevertheless seek to bring a claim in a venue other than those designated in the exclusive forum provisions. In such instance, we would expect to vigorously assert the validity and enforceability of the exclusive forum provisions of our second amended and restated bylaws. This may require significant additional costs associated with resolving such action in other jurisdictions and there can be no assurance that the provisions will be enforced by a court in those other jurisdictions.

These exclusive forum provisions may limit the ability of our stockholders to bring a claim in a judicial forum that such stockholders find favorable for disputes with us or our directors, officers or employees, which may discourage such lawsuits against us and our directors, officers and employees. If a court were to find the exclusive forum provision contained in our second amended and restated bylaws to be inapplicable or unenforceable in an action, we may incur further significant additional costs associated with resolving such action in other jurisdictions, all of which could materially adversely affect our business, financial condition and operating results.

We may not be able to continue to satisfy listing requirements of the Nasdaq Global Select Market or maintain a listing of our common stock on the Nasdaq Global Select Market.

Our common stock is listed on the Nasdaq Global Select Market. We must meet certain financial and liquidity criteria to maintain such listing. If we violate or fail to meet any of the Nasdaq Global Select Market's listing standards, our common stock may be delisted. In addition, our board of directors may determine that the cost of maintaining our listing on a national securities exchange outweighs the benefits of such listing. A delisting of our common stock from the Nasdaq Global Select Market may materially impair our stockholders' ability to buy and sell our common stock and could have an adverse effect on the market price of, and the efficiency of the trading market for, our common stock. The delisting of our common stock could significantly impair our ability to raise capital and the value of your investment.

General Risk Factors

Changes in tax laws or regulations or in their implementation or interpretation may adversely affect our business and financial condition.

New income, sales, use or other tax laws, statutes, rules, regulations or ordinances could be enacted at any time, which could adversely affect our business or financial condition. Further, existing tax laws, statutes, rules, regulations or ordinances could be interpreted, changed, modified or applied adversely to us. A number of other factors could materially adversely affect our business and financial condition including: tax policy initiatives and reforms under consideration (such as those related to the Organization for Economic Co-Operation and Development's, or OECD, Base Erosion and Profit Shifting, or BEPS, Project, the European Commission's state aid investigations and other initiatives), the practices of tax authorities in jurisdictions in which we operate; the resolution of issues arising from tax audits or examinations and any related interest or penalties. Such changes may include (but are

not limited to) the taxation of operating income, investment income, dividends received or (in the specific context of withholding tax) dividends paid.

The OECD Pillar Two Model Rules established a minimum global effective tax rate of 15% on country-by-country basis. EU member states along with many other countries adopted or expected to adopt the OECD Pillar Two Model effective January 1, 2024 or thereafter. The OECD and other countries continue to publish guidelines and legislation which include transition and safe harbor rules. We continue to monitor new legislative changes and assess the global impact of the Pillar Two Model Rules. Based on our initial assessment, we anticipate Pillar Two top-up taxes to be immaterial.

The U.S. government may enact significant new changes to the taxation of business entities including, among others, an increase in the corporate income tax rate. Furthermore, the rules dealing with U.S. federal, state, and local income taxation are constantly under review by persons involved in the legislative process and by the Internal Revenue Service, or IRS, and the U.S. Treasury Department. Changes to tax laws (which changes may have retroactive application) could adversely affect us or holders of our common stock. In recent years, many such changes have been made and changes are likely to continue to occur in the future. Future changes in tax laws could have a material adverse effect on our business, cash flow, financial condition or results of operations. We urge investors to consult with their legal and tax advisers regarding the implications of potential changes in tax laws on an investment in our common stock.

We are unable to predict what tax reform may be proposed or enacted in the future or what effect such changes would have on our business, but such changes, to the extent they are brought into tax legislation, regulations, policies or practices in jurisdictions in which we operate, could increase the estimated tax liability that we have expensed to date and paid or accrued on our balance sheets, and otherwise affect our financial position, future results of operations, cash flows in a particular period and overall or effective tax rates in the future in countries where we have operations, reduce post-tax returns to our shareholders and increase the complexity, burden and cost of tax compliance.

Tax authorities may disagree with our positions and conclusions regarding certain tax positions, or may apply existing rules in an unforeseen manner, resulting in unanticipated costs, taxes or non-realization of expected benefits.

A tax authority may disagree with tax positions that we take, which could result in increased tax liabilities. For example, His Majesty's Revenue & Customs, the IRS or another tax authority could challenge our allocation of income by tax jurisdiction and the amounts paid between our affiliated companies pursuant to our intercompany arrangements and transfer pricing policies, including amounts paid with respect to our intellectual property development. Similarly, a tax authority could assert that we are subject to tax in a jurisdiction where we believe we have not established a taxable connection, often referred to as a "permanent establishment" under international tax treaties, and such an assertion, if successful, could increase our expected tax liability in one or more jurisdictions. A tax authority may take the position that material income tax liabilities, interest and penalties are payable by us, in which case we expect that we might contest such assessment. Contesting such an assessment may be lengthy and costly and if we were unsuccessful in disputing the assessment, the implications could increase our anticipated effective tax rate, where applicable.

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

We have a history of cumulative losses and anticipate that we will continue to incur significant losses in the foreseeable future; thus, we do not know whether or when we will generate taxable income necessary to utilize our net operating losses, or NOLs, or research and development tax credit carryforwards. As of December 31, 2024, we had federal NOLs of \$58.2 million and state NOL carryforwards of \$76.6 million. We did not generate U.K. NOLs in 2024, and do not anticipate any going forward as our U.K. entity, PepGen Limited, was dissolved on December 10, 2024.

As a company that carries out extensive research and development activities, we sought to benefit from the U.K. research and development tax relief programs, being the Small and Medium-sized Enterprises R&D tax relief program, or SME Program, and, to the extent that our projects are grant funded or relate to work subcontracted to the company by third parties, the Research and Development Expenditure Credit program, or RDEC Program. Under the SME Program, we may be able to surrender the trading losses that arise from our qualifying research and development activities for a cash rebate of approximately 33.4% of the surrenderable losses. The majority of our research and development activities during 2021 were eligible for inclusion within these tax credit cash rebate claims. We may not be able to continue to claim payable research and development tax credits in the future if we cease to qualify as an SME, based on size criteria concerning employee headcount, turnover and gross assets or if we no longer conduct qualifying research and development activities through our wholly-owned subsidiary PepGen Limited. The U.K. Finance Act of 2021 introduced a cap on payable credit claims under the SME Program in excess of £20,000 with effect from April 2021 by reference to, broadly, three times the total PAYE and NICs liability of the company, subject to an exception which prevents the cap from applying. That exception requires the company to be creating, taking steps to create or managing intellectual property, as well as having qualifying research and development expenditure in respect of connected parties which does not exceed 15% of the total qualifying expenditure. If such exception does not apply, this could restrict the amount of credit that we are able to claim. For the year ended

December 31, 2024, our research and development tax credits from the U.K. government were not material as the intellectual property was transferred from our wholly-owned U.K. subsidiary, PepGen Limited, to the parent company, PepGen Inc. in January 2022.

For U.S. federal income tax purposes, in general, under Sections 382 and 383 of the U.S. Internal Revenue Code of 1986, as amended, or the Code, and corresponding provisions of state law, a corporation that undergoes an “ownership change,” generally defined as a greater than 50 percentage point change (by value) in its equity ownership by certain stockholders over a three-year period, is subject to limitations on its ability to utilize its pre-change NOLs and pre-change research and development tax credit carryforwards to offset post-change income or taxes. We have not conducted a study to assess whether any such ownership changes have occurred. We may experience such ownership changes in the future. As a result, if, and to the extent that, we earn net taxable income, our ability to use our NOL carryforwards and research and development tax credit carryforwards to offset such taxable income may be subject to limitations.

Additionally, the use of the U.K. NOL carryforwards could be restricted, under Part 14 of the Corporation Tax Act 2010, if a “change in ownership” of either PepGen Inc. or PepGen Limited were to occur and certain other conditions are met. A “change in ownership” is defined, broadly, as the acquisition by one or more persons of more than half of the ordinary share capital of a company. The use of the U.K. NOL carryforwards could be restricted if, within a certain period of a change in ownership, there is a major change in the conduct of PepGen Limited’s trade, PepGen Limited’s trading activities become small or negligible, or if certain other conditions are met.

Any restructuring or change in the nature of our operations of our company may give rise to tax liabilities and/or restrictions in the amount and/or availability of tax attributes.

We have undergone, and may in the future undertake, changes in the nature or conduct of our operations. For example, pursuant to an asset transfer agreement effective as of January 1, 2022, we effected a novation of all intellectual property assets of our wholly-owned U.K. subsidiary PepGen Limited to PepGen Inc., which resulted in the recording of a tax charge of \$3.7 million, including \$0.7 million related to an uncertain tax position. PepGen Limited was dissolved on December 10, 2024 and we recognized a \$0.7 million tax benefit associated with the resolution of the uncertain tax position. Any future actions regarding transfer of assets from our U.K. subsidiary or other potential international subsidiaries could give rise to tax liabilities for us and/or to the erosion of our tax attributes (such as NOLs).

Our disclosure controls and procedures may not prevent or detect all errors or acts of fraud.

We are subject to certain reporting requirements of the Exchange Act. Our disclosure controls and procedures are designed to reasonably assure that information required to be disclosed by us in reports we file or submit under the Exchange Act is accumulated and communicated to management, recorded, processed, summarized and reported within the time periods specified in the rules and forms of the SEC. We believe that any disclosure controls and procedures or internal controls and procedures, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. These inherent limitations include the realities that judgments in decision-making can be faulty, and that breakdowns can occur because of simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by an unauthorized override of the controls. Accordingly, because of the inherent limitations in our control system, misstatements or insufficient disclosures due to error or fraud may occur and not be detected.

As a public company, we may be at an increased risk of securities class action litigation.

Historically, 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 for us because biotechnology and pharmaceutical companies have experienced significant stock price volatility in recent years. If we were to be sued, it could result in substantial costs and a diversion of management’s attention and resources, which could harm our business.

We may be exposed to significant foreign exchange risk.

We incur portions of our expenses, and may in the future derive revenues, in a variety of currencies. As a result, we are exposed to foreign currency exchange risk as our results of operations and cash flows are subject to fluctuations in foreign currency exchange rates. Fluctuations in currency exchange rates have had, and will continue to have, an impact on our results as expressed in U.S. dollars. We currently do not engage in hedging transactions to protect against uncertainty in future exchange rates between particular foreign currencies and the euro. We cannot predict the impact of foreign currency fluctuations, and foreign currency fluctuations in the future may adversely affect our financial condition, results of operations and cash flows.

Item 1B. Unresolved Staff Comments.

None.

Item 1C. Cybersecurity

Cyber Risk Management and Strategy

We have processes for assessing, identifying, and managing cybersecurity risks, which are built into our information technology function and are designed to help protect our information assets and operations from internal and external cyber threats, protect employee and clinical trial information from unauthorized access or attack, as well as secure our networks and systems. Such processes include physical, procedural, and technical safeguards, and routine review of our policies and procedures in an effort to identify risks and refine our practices. We engage certain external parties, including a contracted information technology consultant who is dedicated to our organization, to enhance our cybersecurity oversight.

In an effort to deter and detect cyber threats, we perform annual phishing tests with employees. We also require annual cybersecurity and prevention training for employees, which may cover topics such as social engineering, phishing, password protection, confidential data protection, and mobile security, and is designed to educate employees on incident reporting. We also use technology-based tools, including third-party tools and solutions, designed to mitigate cybersecurity risks and to bolster our employee-based cybersecurity programs.

We have not identified any cybersecurity incidents or threats that have materially affected us or are reasonably likely to materially affect us, including our business strategy, results of operations or financial condition; however, like other companies in our industry, we and our third-party vendors may, from time to time, experience threats and security incidents relating to our and our third-party vendors' information systems. For more information, see *"Risk Factors-Risks Related to Employee Matters, Managing Growth and Other Operational Matters -Our internal information technology systems, or those of our vendors, collaborators or other contractors or consultants, may fail or suffer security breaches, loss or leakage of data and other disruptions or compromise, which could result in a material disruption of our product development programs, compromise sensitive information related to our business or prevent us from accessing critical information, or trigger contractual and legal obligations, potentially exposing us to liability, reputational harm or otherwise adversely affecting our business and financial results."*

Governance Related to Cybersecurity Risks

Our audit committee of the board of directors, or the Audit Committee, is responsible for overseeing cybersecurity risk, pursuant to the Audit Committee charter, and periodically updates our board of directors on such matters. The Audit Committee receives periodic updates from management and our contracted information technology consultant regarding cybersecurity matters. We have a process for the Audit Committee to be notified between such updates in the event of any significant new cybersecurity threats or incidents.

Management is responsible for, and is forming a committee tasked with, the operational oversight of company-wide cybersecurity strategy, policy, and standards across relevant departments to assess and help prepare us to address cybersecurity risks. Our contracted information technology consultant, supported by management, oversees the day-to-day implementation and management of our cybersecurity program. Our information technology consultant reports to the Chief Financial Officer, who currently operates as our head of information technology. Our information technology consultant has approximately 20 years of experience in information technology, and also leverages the experience of a third-party managed systems provider. Our information technology consultant regularly reports to the Chief Financial Officer as well as to other executive management, including our General Counsel, on cyber matters, as appropriate.

Item 2. Properties.

Our principal facility is located at 321 Harrison Ave, Boston, Massachusetts, where we lease and occupy approximately 31,668 square feet of office and laboratory space. The lease was signed on December 1, 2021 and the lease term commenced on December 29, 2022. The current term of our lease expires in May 2032, with an option to extend the lease for one successive five-year term. We believe our facilities are adequate and suitable for our current needs and that should it be needed, suitable additional or alternative space will be available to accommodate our operations.

Item 3. Legal Proceedings.

From time to time, we may be a party to litigation or subject to claims incident to the ordinary course of business. Although the results of litigation and claims cannot be predicted with certainty, we currently believe that the final outcome of these ordinary course matters will not have a material adverse effect on our business. Regardless of the outcome, litigation can have an adverse impact on us

because of defense and settlement costs, diversion of management resources and other factors. As of December 31, 2024, we were not a 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.

Market Information

Our common stock has traded on the Nasdaq Global Select Market under the symbol “PEPG” since May 10, 2022. Prior to that date, there was no public trading market for our common stock.

Holders

As of February 18, 2025, we had 11 holders of record of our common stock. The actual number of stockholders is greater than the number of record holders, and includes stockholders who are beneficial owners, but whose shares are held in street name by brokers and other nominees. The number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

Dividend Policy

We have never declared or paid cash dividends on our common stock since our inception. We currently intend to retain all available funds and any future earnings to fund the development and expansion of our business, and we do not anticipate paying any cash dividends in the foreseeable future. Any future determination to declare and pay dividends will be made at the discretion of our board of directors and will depend on then-existing conditions, including our results of operations, financial condition, contractual restrictions, capital requirements, business prospects and other factors our board of directors may deem relevant.

Securities Authorized for Issuance Under Equity Compensation Plans

Information about our equity compensation plans is incorporated by reference herein to Item 12 Part III of this 10-K.

Unregistered Sales of Equity Securities

None.

Use of Proceeds

On May 10, 2022, we closed our IPO in which we sold an aggregate of 9,000,000 shares at a public offering price of \$12.00 per share for gross proceeds of \$108.0 million. In connection with the IPO, we granted the underwriters a 30-day option to purchase 1,350,000 additional shares of common stock. On May 16, 2022, the underwriters exercised the option in part and we issued 1,238,951 shares of our common stock for gross proceeds of \$14.9 million. From the IPO and option exercise by the underwriters, we received approximately \$122.9 million in gross proceeds and \$110.2 million in net proceeds, after deducting underwriting discounts and offering expenses payable by us. None of the underwriting discounts and commissions or offering expenses were incurred or paid, directly or indirectly, to any of our directors or officers or their associates or to persons owning 10% or more of our common stock or to any of our affiliates.

The offer and sale of all of the shares of our common stock in our IPO were registered under the Securities Act pursuant to a registration statement on Form S-1, as amended (File No. 333- 264335), which was declared effective by the SEC on May 5, 2022. BofA Securities, Inc., SVB Securities LLC, Stifel, and Wedbush Securities Inc. acted as underwriters for the IPO.

Item 6. [Reserved].

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

You should read the following discussion and analysis of our financial condition and results of operations together with our financial statements and the related notes included elsewhere in this 10-K. Some of the information contained in this discussion and analysis or set forth elsewhere in this 10-K, including information with respect to our plans, strategies, objectives, expectations and intentions for our business and related financing, includes forward-looking statements that involve risks and uncertainties. As a result of many factors, including those factors set forth in the "Risk Factors" section of this 10-K, our actual results could differ materially from the results described in or implied by these forward-looking statements. Please also see the section titled "Special Note Regarding Forward-Looking Statements."

Overview

PepGen is a clinical-stage biotechnology company advancing the next-generation of oligonucleotide therapies with the goal of transforming the treatment of severe neuromuscular and neurological diseases. Our proprietary EDO platform is founded on over a decade of research and development and leverages CPPs to improve the uptake and activity of conjugated oligonucleotide therapeutics. Using these EDO peptides, we are generating a pipeline of oligonucleotide therapeutic candidates that are designed to target the root cause of serious diseases.

We are initially focused on addressing the underlying cause of DMD and DM1, that have high unmet need. Our current pipeline consists of two clinical stage programs, PGN-EDO51 for DMD patients who are amenable to an exon 51-skipping approach and PGN-EDODM1 for DM1 patients, along with several additional preclinical stage programs. We anticipate expanding this pipeline over time to include other neuromuscular targets as well as potential opportunities in neurologic diseases.

We completed a first-in-human Phase 1 clinical trial in HVs with our initial product candidate, PGN-EDO51, in the third quarter of 2022. In the Phase 1 HV clinical trial, treatment with PGN-EDO51 resulted in high levels of exon skipping in humans following a single dose. Our ongoing clinical development program for PGN-EDO51 is comprised of two parallel Phase 2 studies of PGN-EDO51 in DMD patients. The first study, CONNECT1, is an ongoing open-label MAD study in boys and young men living with DMD amenable to exon 51 skipping being conducted in Canada. In July 2024, we reported initial clinical data from the CONNECT1 study from the 5 mg/kg starting dose cohort, which we believe demonstrate a favorable emerging safety profile and promising early exon skipping and dystrophin production. All participants from the first cohort have continued in the LTE portion of the study. We have fully enrolled the 10 mg/kg dose cohort in CONNECT1 and expect to report initial safety, exon skipping and dystrophin production data from this cohort by the end of the third quarter of 2025.

We have received communication from Health Canada that dosing of participants in the 5 and 10 mg/kg cohorts may continue at their current dose levels. Health Canada has requested additional information from us to address its safety concerns before any further dose escalation or enrollment of any additional participants at the current dose levels. We are working with Health Canada to address its questions.

The second Phase 2 study of PGN-EDO51, CONNECT2, is a randomized, double-blind, placebo-controlled MAD study in boys and young men living with DMD amenable to exon 51 skipping, currently open in the U.K. We recently received a clinical hold notice from the FDA regarding our IND application to initiate the CONNECT2 study in the U.S. We are working with the FDA to address its questions regarding supportive data for the dosing levels planned for the patient population. In parallel, we are evaluating opening CONNECT2 in other geographies outside of the U.S., subject to regulatory authorizations.

The CONNECT2 study will evaluate multiple dose cohorts and trial participants will be administered PGN-EDO51 once every four weeks for six months. We will assess safety, tolerability, exon skipping, dystrophin expression and functional outcomes in this study. The CONNECT2 study, together with data from the CONNECT1 study, is intended to support a potential accelerated approval pathway for PGN-EDO51, subject to regulatory authority feedback.

The FDA has granted both orphan drug designation and RPDD for PGN-EDO51 for the treatment of DMD patients who are amenable to exon 51 skipping.

We are also developing PGN-EDODM1 for the treatment of DM1 and are utilizing what we believe to be a unique mechanism of action and a different delivery approach compared to other approaches in more advanced stages of clinical development. We have conducted extensive preclinical studies of our product candidate, and these preclinical data form the basis of our clinical development plan for PGN-EDODM1. Our clinical development program for PGN-EDODM1 includes two studies, FREEDOM, a multinational, randomized, double-blind, placebo-controlled Phase 1 SAD study, and FREEDOM2, a multinational, randomized, double blind, placebo-controlled Phase 2 MAD study. In the FREEDOM study, we are enrolling adult participants with DM1 in multiple geographies including the U.S., U.K. and Canada, to evaluate the safety and tolerability of PGN-EDODM1, as well as oligonucleotide muscle concentrations, splicing correction and functional outcome measures at day 28 and at week 16 following a single dose of PGN-EDODM1. On February 24, 2025, we reported initial data from the 5 mg/kg and 10 mg/kg dose cohorts in this study. PGN-EDODM1 was observed to have a favorable emerging safety profile and robust splicing correction in a dose-dependent manner in the 5 and 10 mg/kg dose cohorts. We expect to report data from the 15 mg/kg cohort of the FREEDOM study in the second half of 2025.

The safety data from the ongoing FREEDOM study has informed the design of FREEDOM2, which is currently open in Canada and U.K. We also plan to open the FREEDOM2 study other geographies, including the U.S., subject to regulatory authorizations. FREEDOM2 is a Phase 2 randomized, double-blind, placebo-controlled MAD study of PGN-EDODM1 in DM1 patients. FREEDOM2 is designed to assess PGN-EDODM1's safety and tolerability, splicing correction and functional outcome measures in DM1 patients. We expect to report data from the 5 mg/kg cohort of the FREEDOM2 study in the first quarter of 2026.

The FDA has granted both orphan drug designation and Fast Track designation for PGN-EDODM1 for the treatment of DM1.

In addition to these lead candidates, we are evaluating EDO candidates for additional DMD sub-populations amenable to skipping of other exons, including exon 53, 45 and 44. In the future, we intend to apply our deep understanding of our EDO platform and PMO therapeutics to the development of additional product candidates in other indications.

Initial Public Offering, Follow-on Offering and Liquidity

In May 2022, we closed our IPO, in which we sold an aggregate of 9,000,000 shares of common stock at a public offering price of \$12.00 per share for gross proceeds of \$108.0 million. In connection with the IPO, we granted the underwriters a 30-day option to purchase 1,350,000 additional shares of common stock, which they exercised in part to purchase 1,238,951 additional shares of common stock for gross proceeds of \$14.9 million. We received approximately \$122.9 million in gross proceeds and \$110.2 million in net proceeds in the IPO, after deducting underwriters' fees and offering expenses.

Immediately prior to consummation of the IPO, all 12,546,805 outstanding shares of our redeemable convertible preferred stock, and 35,529 preferred stock warrants that were exercised on May 4, 2022, converted into 12,359,856 shares of our common stock.

On February 5, 2024, we issued and sold 1,000,000 of common stock shares at a purchase price of \$10.00 per share under our ATM program, pursuant to the Sales Agreement with Stifel, resulting in net proceeds of \$9.9 million. On February 9, 2024, we issued and sold 7,530,000 shares of common stock at a purchase price of \$10.635 per share, which was the closing sale price of our common stock on the Nasdaq Global Select Market on February 6, 2024, in the Follow-on Offering. The Follow-on Offering resulted in net proceeds of \$76.4 million after deducting underwriters' fees of \$3.7 million. Net proceeds from the ATM program and Follow-on Offering, after deducting underwriters' fees and costs of the offerings, were \$86.3 million.

Since our inception, we have not generated any revenue from product sales or other sources and have incurred significant operating losses and negative cash flows from our operations. Our primary uses of cash to date have been to fund our research and development activities, business planning, establishing and maintaining our intellectual property portfolio, acquiring and developing product and technology rights, hiring personnel, leasing premises and associated capital expenditures, raising capital, and providing general and administrative support for these operations. To date, we have funded our operations primarily through private placements of our convertible preferred stock and proceeds from our IPO, the ATM program and the Follow-on Offering.

We have incurred operating losses in each year since our inception. Our net losses were \$90.0 million and \$78.6 million for the years ended December 31, 2024 and December 31, 2023, respectively. As of December 31, 2024, we had cash, cash equivalents, and marketable securities of \$120.2 million. As of December 31, 2024, we had an accumulated deficit of \$271.5 million. We expect our expenses and operating losses will continue as we conduct our ongoing preclinical studies and current and planned clinical trials, continue our research and development activities, utilize third parties to manufacture our product candidates and related raw materials, hire additional personnel, protect our intellectual property and incur additional costs associated with being a public company, including audit, legal, regulatory, and tax-related services associated with maintaining compliance with an exchange listing and SEC requirements, director and officer insurance premiums, and investor relations costs. In addition, we have several development, regulatory and commercial milestone payment obligations under our licensing arrangements. Our net losses may fluctuate significantly from quarter-to-quarter and year-to-year, depending on the timing of our preclinical studies, current and planned clinical trials, manufacturing campaigns and our expenditures on other research and development activities.

Based on our currently planned operations, we believe that our existing cash, cash equivalents and marketable securities will be sufficient to fund our operations for at least 12 months from the date of the filing of this 10-K. We do not expect to generate any revenues from product sales unless and until we successfully complete development and obtain regulatory approval for one or more of our product candidates, which will not be for at least the next several years, if ever. If we obtain regulatory approval for any of our product candidates, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution. Accordingly, until such time as we can generate significant revenue from sales of our product candidates, if ever, we expect to finance our cash needs through equity offerings, debt financings or other capital sources, including potential collaborations, licenses and other similar arrangements. However, we may be unable to raise additional funds or enter into such other arrangements when needed on favorable terms or at all. Our failure to raise capital or enter into such other arrangements when needed would have a negative impact on our financial condition and could force us to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Corporate Reorganization

We were initially formed as PepGen Limited on January 25, 2018, in the U.K. On November 9, 2020, PepGen Limited initiated a corporate reorganization, or the Reorganization. As part of the Reorganization, PepGen Limited formed PepGen Inc., a Delaware corporation with nominal assets and liabilities, for the purpose of consummating the Reorganization. In connection with the Reorganization, the existing shareholders of PepGen Limited exchanged each of their classes of shares of PepGen Limited for the same number and class of common stock of PepGen Inc. on a one-to-one basis. The newly issued stock of PepGen Inc. had substantially identical rights to the exchanged shares of PepGen Limited. As a result of the exchange, PepGen Inc. became the sole shareholder of PepGen Limited. Upon the completion of the Reorganization on November 23, 2020, the historical financial statements of PepGen Limited became the historical financial statements of PepGen Inc., as the Reorganization was deemed to be between entities under common control.

After the Reorganization was completed, PepGen Limited began the process of transferring certain operations, including financial management functions, to PepGen Inc. pursuant to an intercompany services agreement, effective as of April 2021, and certain assets, including a novation of all intellectual property assets, pursuant to an asset transfer agreement, effective as of January 1, 2022. After the transfer of intellectual property and other assets from PepGen Limited to PepGen Inc., there were limited operations through the end of 2022 at PepGen Limited. PepGen Limited was dissolved on December 10, 2024.

Components of Results of Operations

Operating Expenses

Research and Development

To date, our research and development expenses have primarily consisted of external and internal costs associated with our research and development activities, including our discovery and research efforts, the development of our proprietary EDO platform, and the preclinical and clinical development of our product candidates. Our research and development expenses include:

- external expenses, including expenses incurred under arrangements with third parties, such as CROs, CDMOs, consultants and our scientific advisors;
- personnel-related costs, including salaries, cash incentive compensation, payroll taxes, employee benefits, and stock-based compensation;
- costs for laboratory supplies and materials and reagents for chemical synthesis of product candidates; and
- facility costs, depreciation, and other expenses, which include direct and allocated expenses for rent and maintenance of facilities, insurance, and other supplies.

Research and development expenses are recognized as incurred and payments made prior to the receipt of goods or services to be used in research and development activities are recorded as prepaid expenses until the goods or services are received. The following table (in thousands) summarizes our research and development expenses for the years ended December 31, 2024 and December 31, 2023. The direct external development program expenses reflect external costs attributable to our clinical development candidates and preclinical candidates selected for further development. Our internal resources, personnel and infrastructure are not directly tied to any one research or drug discovery program and are deployed across multiple programs. As such, we do not track internal expenses on a program-specific basis

	Year Ended December 31,	
	2024	2023
External expenses:		
PGN-EDO51	\$ 19,195	\$ 21,369
PGN-EDODM1	21,265	16,486
Other programs and unallocated expenses	2,556	4,762
Total external expense	43,016	42,617
Internal expenses:		
Personnel-related (including stock-based compensation)	23,433	16,143
Facilities and related costs	5,819	5,165
Other	4,210	4,201
Total research and development expenses	<u>\$ 76,478</u>	<u>\$ 68,126</u>

We expect that our research and development expenses will increase in 2025, as compared to 2024, as we conduct our ongoing Phase 2 clinical trials for PGN-EDO51 and our ongoing Phase 1 and Phase 2 clinical trials of PGN-EDODM1. We also continue to

increase our research and development headcount to support these programs. Research and development expenses for our lead programs can be variable quarter-over-quarter due to the timing of manufacturing campaigns, which are accounted for under the percentage of completion method. The process of conducting preclinical studies and clinical trials necessary to obtain regulatory approval is costly and time consuming. We may never succeed in achieving marketing approval for any of our product candidates.

The timelines and costs associated with research and development activities are uncertain and can vary significantly for each product candidate and development program due to the inherently unpredictable nature of preclinical and clinical development. We anticipate we will make determinations as to which programs to pursue and how much funding to direct to each program on an ongoing basis in response to preclinical and clinical results, regulatory developments, and ongoing assessments as to each program's commercial potential. We will need to raise substantial additional capital in the future.

Our future development costs may vary significantly based on factors such as:

- the status of clinical trials, the timing and costs, if any, associated with resolving a clinical hold, animal and other preclinical studies and IND- or CTA-enabling studies;
- per patient trial costs;
- the number of trials required for approval;
- the number of sites included in the trials;
- the countries in which the trials are conducted;
- the length of time required to enroll eligible patients;
- the number of patients that participate in the trials;
- the number of doses that patients receive;
- the drop-out or discontinuation rates of patients;
- the duration of patient participation in the trials and follow-up;
- the cost and timing of manufacturing our product candidates and the cost and timing of our manufacturing campaigns;
- the efficacy and safety profile of our product candidates; and
- maintaining a continued acceptable safety profile of our products if any receive regulatory approval.

General and Administrative

General and administrative expenses consist primarily of personnel-related costs, including salaries, cash incentive compensation, payroll taxes, employee benefits, and stock-based compensation charges for those individuals in executive, finance, facility operations, and other administrative functions. Other significant costs include legal fees relating to intellectual property and corporate matters, professional fees for audit, accounting and consulting services, and insurance costs.

We anticipate that our general and administrative expenses will increase in 2025 as compared to 2024 primarily due to personnel costs, including stock-based compensation expense. Other general and administrative expenses will remain consistent to support our public company operating expenses associated with audit, legal, regulatory, and tax-related services associated with maintaining compliance with our exchange listing and SEC requirements, director and officer insurance premiums, and investor relations.

Other Income (Expense), Net

Interest Income

Interest income consists of interest earned on our money market mutual funds and short-term U.S. treasury holdings.

Other Income (expense)

Other components of other income (expense) relate to realized and unrealized gains and losses on currency revaluation.

Income Taxes

We recognized a tax benefit for the year ended December 31, 2024 due to the derecognition of an unrecognized tax benefit of \$0.7 million upon the dissolution of our U.K.-based entity, PepGen Limited on December 10, 2024. Additionally, we recorded \$0.1 million in state taxes on interest income generated from the Company's cash equivalents and marketable securities. We have not recorded a U.S. provision for federal or state income taxes as we have no revenue and have incurred losses since inception.

Results of Operations

Comparison of the Year Ended December 31, 2024 and 2023

The following table summarizes our results of operations for the years ended December 31, 2024 and 2023 (in thousands):

	Year Ended December 31,		Period-to- Period Change
	2024	2023	
Operating expenses:			
Research and development	\$ 76,478	\$ 68,126	\$ 8,352
General and administrative	21,261	16,640	4,621
Total operating expenses	\$ 97,739	\$ 84,766	\$ 12,973
Operating loss	\$ (97,739)	\$ (84,766)	\$ (12,973)
Other income (expense), net			
Interest income	7,142	6,400	742
Other (expense) income, net	(1)	(187)	186
Total other income (expense), net	7,141	6,213	\$ 928
Net loss before income tax	\$ (90,598)	\$ (78,553)	\$ (12,045)
Income tax benefit (expense)	617	(73)	690
Net loss	<u>\$ (89,981)</u>	<u>\$ (78,626)</u>	<u>\$ (11,355)</u>

Research and Development Expenses

Research and development expenses increased by \$8.4 million from \$68.1 million for the year ended December 31, 2023, to \$76.5 million for the year ended December 31, 2024. This increase was attributable to expenses related to the advancement of clinical trials for our two lead programs, including a \$7.6 million increase in clinical trial costs, a \$0.7 million increase in manufacturing costs, and a \$7.3 million increase in personnel-related costs, inclusive of an increase of \$2.0 million in stock-based compensation expense. Additionally, there was an increase of \$0.7 million in facility and other office related expenses, including depreciation, a \$1.0 million increase in consulting expense, and a \$0.3 million increase in other R&D expenses, primarily related to insurance expense. These increases were partially offset by a \$9.3 million decrease in preclinical costs as our two lead programs are now in clinical trials.

General and Administrative Expenses

General and administrative expenses increased by \$4.6 million from \$16.6 million for the year ended December 31, 2023, to \$21.3 million for the year ended December 31, 2024. The increase was driven primarily by an increase of \$4.3 million in personnel-related costs due to increased headcount, inclusive of \$2.4 million in stock-based compensation expense, and an increase of \$0.6 million in facility and office related expenses related to rent expense for our operating lease and depreciation on office furniture. These increases were partially offset by a \$0.3 million decrease in insurance expense.

Other Income (Expense), Net

Other income (expense), net was income of \$7.1 million for the year ended December 31, 2024, compared to income of \$6.2 million for the year ended December 31, 2023. The increase was primarily driven by interest earned from our money market fund and U.S. treasury holdings.

Income Tax Benefit (Expense)

Income tax benefit was a net benefit of \$0.6 million for the year ended December 31, 2024 related the derecognition of an unrecognized tax benefit of \$0.7 million upon the dissolution of our U.K.-based entity, PepGen Limited in December 2024. This is partially offset by \$0.1 million in state taxes on interest income generated from the Company's cash equivalents and marketable securities. Income tax expense was \$0.1 million for the year ended December 31, 2023.

Liquidity and Capital Resources

Sources of Liquidity

From our inception in January 2018 through December 31, 2024, we have funded our operations primarily through the sale of our common stock and convertible preferred stock. We received aggregate gross proceeds of \$163.9 million from these sales prior to our IPO. Additionally, in May 2022, we received gross proceeds from our IPO of \$122.9 million.

On June 2, 2023, we filed a shelf registration statement on Form S-3 with the SEC, which covers the offering, issuance and sale of an amount up to \$300.0 million in the aggregate of shares of our common stock, preferred stock, debt securities, warrants, and/or units or any combination thereof, which was declared effective on June 16, 2023.

On August 8, 2023, we filed a prospectus supplement and entered into the Sales Agreement with Stifel, as sales agent, which provides for the issuance and sale by us of up to \$100.0 million of shares of common stock from time to time under the ATM program. On February 5, 2024, we issued and sold 1,000,000 shares of common stock at a purchase price of \$10.00 per share under the ATM program, resulting in net proceeds of \$9.9 million.

On February 9, 2024, we issued and sold 7,530,000 shares of common stock in the Follow-on Offering at a purchase price of \$10.635 per share, resulting in net proceeds of \$76.4 million after deducting underwriters' fees and offering costs of \$3.7 million.

On June 28, 2024, we filed a second shelf registration statement on Form S-3 with the SEC, which covers the offering, issuance and sale of an amount up to \$250.0 million in the aggregate of shares of our common stock, preferred stock, debt securities, warrants, and/or units or any combination thereof, which was declared effective on July 8, 2024.

Future Funding Requirements

As of December 31, 2024, we had cash, cash equivalents, and marketable securities of \$120.2 million. Based on our currently planned operations, we believe that our existing cash, cash equivalents, and marketable securities will be sufficient to fund our operations for at least 12 months from the date of the filing of this 10-K. However, our forecast of the period of time through which our financial resources will be adequate to support our operations is a forward-looking statement that involves risks and uncertainties, and actual results could vary materially. We have based this estimate on assumptions that may prove to be wrong, and we could deplete our capital resources sooner than we expect. Additionally, the process of conducting preclinical studies and testing product candidates in clinical trials is costly, and the timing of progress and expenses in these studies and trials is uncertain.

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

- the scope, progress, costs and results of preclinical and clinical development for our product candidates, any additional product candidates we may develop and any new indications we may pursue;
- the scope, costs, timing and outcome of regulatory review of our product candidates, any additional product candidates we may develop and any new indications we may pursue;
- the cost and timing of manufacturing activities;
- the identification of additional research programs and product candidates;
- the costs and scope of the continued development of our EDO platform;
- the costs and timing of preparing, filing and prosecuting applications for patents, maintaining and enforcing our intellectual property rights and defending any intellectual property-related claims, including claims of infringement, misappropriation or other violations of third-party intellectual property;
- the costs and timing of future commercialization activities, including product manufacturing, marketing, sales and distribution, for any product candidate that receives marketing approval;
- the costs of satisfying any post-marketing requirements;
- the revenue, if any, received from commercial sales of our product candidates if marketing approval is received;
- the costs of operational, financial and management information systems and associated personnel;
- the associated costs in connection with any acquisition of in-licensed products, intellectual property and technologies; and
- the costs of operating as a public company.

Until such time, if ever, as we can generate substantial product revenue to support our cost structure, we expect to finance our cash needs through equity offerings, debt financings, or other capital sources, potentially including collaborations, licenses, and other similar arrangements. However, we may be unable to raise additional funds or enter into such other arrangements when needed on

favorable terms or at all. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our stockholders will be or could be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our common stockholders. Debt financing and 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 funds through collaborations, or other similar arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or drug candidates or grant licenses on terms that may not be favorable to us and/or may reduce the value of our common stock. Our failure to raise capital or enter into such other arrangements when needed could have a negative impact on our financial condition and on our ability to pursue our business plans and strategies. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market our drug candidates even if we would otherwise prefer to develop and market such drug candidates ourselves.

Cash Flows

The following table sets forth a summary of the net cash flow activity for the years ended December 31, 2024 and December 31, 2023 (in thousands):

	Year Ended December 31,	
	2024	2023
Net cash (used in) provided by:		
Operating activities	\$ (82,372)	\$ (68,997)
Investing activities	(37,668)	(32,003)
Financing activities	88,749	(189)
Effect of exchange rate changes on cash	(62)	286
Net (decrease) in cash, cash equivalents and restricted cash	<u>\$ (31,353)</u>	<u>\$ (100,903)</u>

Operating Activities

For the year ended December 31, 2024, net cash used in operating activities was \$82.4 million resulting from our net loss of \$90.0 million and by cash provided by changes in our operating assets and liabilities of \$5.3 million partially offset by non-cash charges of \$12.9 million. The net changes in our operating assets and liabilities were primarily due to an increase in prepaids and other current assets of \$1.3 million, a decrease in accrued expenses of \$1.7 million, and a \$3.0 million decrease in operating lease liabilities. These changes were partially offset by a \$0.7 million increase in accounts payable. Non-cash charges included \$11.5 million in stock-based compensation expense, \$3.9 million of accretion of discounts on our marketable securities, \$3.7 million of amortization and interest accretion on our operating lease, and \$1.5 million in depreciation expense.

For the year ended December 31, 2023, net cash used in operating activities was \$69.0 million resulting from our net loss of \$78.6 million partially offset by cash provided by changes in our operating assets and liabilities of \$2.0 million and non-cash charges of \$7.7 million. The net changes in our operating assets and liabilities were primarily due to an increase in accrued expenses of \$1.4 million and an increase in prepaids and other current assets of \$2.0 million. These increases were partially offset by a \$1.2 million decrease in operating lease liabilities related to cash paid towards tenant improvements on our new office and lab lease. Non-cash charges included \$7.0 million in stock-based compensation expense and \$1.2 million in depreciation expense.

Investing Activities

Net cash used in investing activities was \$37.7 million during the year ended December 31, 2024. Cash used in investing activities resulted from \$145.2 million in purchases of marketable securities and \$0.5 million in purchases of property and equipment. This was partially offset by \$108.0 million in maturities and sales of marketable securities.

Net cash used in investing activities was \$32.0 million during the year ended December 31, 2023. Cash used in investing activities was related to \$29.4 million in purchases of marketable securities and \$2.6 million in purchases of property and equipment.

Financing Activities

Net cash provided by financing activities was \$88.7 million for the year ended December 31, 2024, resulting from \$76.9 million in proceeds from the Follow-on Offering, \$9.9 million in proceeds from sales under the Sales Agreement, and \$2.5 million from proceeds from the purchase of shares under employee equity plans, partially offset by \$0.5 million in the payment of deferred offering costs.

Net cash used in financing activities was \$0.2 million for the year ended December 31, 2023, which was primarily the result of \$0.4 million in payments towards offering costs related to our Form S-3 and Sales Agreement filings in May and August 2023, respectively. These payments were partially offset by \$0.3 million of proceeds from the purchase of shares under employee equity plans.

Critical Accounting Policies and Estimates

Our management's discussion and analysis of our financial condition and results of operations are based on our financial statements, which are prepared in accordance with generally accepted accounting principles in the U.S., or GAAP. The preparation of our financial statements requires us to make estimates and assumptions that affect the reported amounts of assets, liabilities, costs, and expenses and the disclosure of contingent assets and liabilities in our financial statements and accompanying notes. We evaluate our estimates and judgments on an ongoing basis. We base our estimates and assumptions on historical experience, known trends and events, and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Our actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are more fully described in Note 2, "*Summary of Significant Accounting Policies*" to our consolidated financial statements appearing elsewhere in this 10-K, we believe that the following accounting policies are the most critical for fully understanding and evaluating our financial condition and results of operations.

Research and Development Expenses and Accrued Research and Development Costs

We are required to estimate our expenses resulting from obligations under contracts with vendors, consultants, CDMOs, and CROs, in connection with conducting research and development activities. The financial terms of these contracts are subject to negotiations, which vary from contract to contract and may result in payment flows that do not match the periods over which materials or services are provided under such contracts. We reflect research and development expenses in our financial statements by matching those expenses with the period in which services and efforts are expended. We account for these expenses according to the progress of the applicable preclinical or clinical study as measured by the timing of various aspects of the study or related activities. We determine accrual estimates through review of the underlying contracts along with preparation of financial models taking into account discussions and confirmations with research and other key personnel and the third-party vendors as to the progress of studies, or other services being conducted. During the course of a study, we adjust our rate of expense recognition if actual results differ from our estimates.

Although we do not expect our estimates to be materially different from amounts actually incurred, if our estimates of the status and timing of services performed differ from the actual status and timing of services performed, it could result in us reporting amounts that are too high or too low in any particular period. To date, there have been no material differences between our estimates of such expenses and the amounts actually incurred.

Stock-Based Compensation

We account for all stock-based compensation awards granted as stock-based compensation expense at fair value in accordance with the Financial Accounting Standards Board ASC Topic 718, *Compensation—Stock Compensation*. Stock-based compensation expense represents the cost of the grant date fair value of equity awards recognized over the requisite service period of the awards (usually the vesting period) on a straight-line or accelerated basis. We estimate the fair value of stock option awards using the Black-Scholes option pricing model and recognize forfeitures as they occur. The fair value of our common stock is used to determine the fair value of restricted stock awards.

The Black-Scholes option pricing model requires the use of subjective assumptions, including the risk-free interest rate, the expected stock price volatility, the expected term of stock options, the expected dividend yield, and the fair value of the underlying common stock on the date of grant. Changes in the assumptions can materially affect the fair value and ultimately how much stock-based compensation expense is recognized. Prior to our IPO, there was no public market for our common stock, and consequently, the estimated fair value of our common stock was determined by our board of directors as of the date of each stock option grant, with input from management, considering third-party valuations of our common stock as well as our board of directors' assessment of additional objective and subjective factors that it believed were relevant and which may have changed from the date of the most recent third-party valuation through the date of the grant. These third-party valuations were performed in accordance with the guidance outlined in the American Institute of Certified Public Accountants' Accounting and Valuation Guide, *Valuation of Privately-Held-Company Equity Securities Issued as Compensation*, or Practice Aid. The Practice Aid identifies various available methods for allocating the enterprise value across classes of series of capital stock in determining the fair value of our common stock at each valuation date. Since our IPO, we have determined the fair market value of our common stock using the closing price of our common stock as reported on the Nasdaq Global Select Market.

The fair value of the common stock underlying stock-based awards is the closing price of the Company's common stock on the date of grant.

Off-balance sheet arrangements

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

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

We are a smaller reporting company as defined by Rule 12b-2 of the Exchange Act and are not required to provide the information required under this item.

Item 8. Financial Statements and Supplementary Data.

Our consolidated financial statements, together with the reports of our independent registered public accounting firms, appear beginning on page F-1 of this 10-K.

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

None.

Item 9A. Controls and Procedures.

Evaluation of Disclosure Controls and Procedures

We maintain disclosure controls and procedures (as defined in Rules 13a-15(e) or 15d-15(e) under the Exchange Act) that are designed to ensure that information required to be disclosed in reports that we file or submit under the Exchange Act is (1) recorded, processed, summarized, and reported within the time periods specified in the SEC's rules and forms and (2) accumulated and communicated to our management, including our principal executive officer and principal financial officer, as appropriate, to allow timely decisions regarding required disclosure.

Our management, with the participation of our principal executive officer and principal financial officer, evaluated the effectiveness of our disclosure controls and procedures as of the end of the period covered by this report. In designing and evaluating our disclosure controls and procedures, our management recognizes that any disclosure controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives, and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Our principal executive officer and principal financial officer have concluded based upon the evaluation described above that, as of December 31, 2024, our disclosure controls and procedures were effective at the reasonable assurance level.

Management's Annual Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act). Our internal control over financial reporting is a process designed under the supervision of our principal executive and principal financial officer to provide reasonable assurance regarding the reliability of our financial reporting and the preparation of financial statements for external purposes in accordance with GAAP. Management assessed our internal control over financial reporting as of December 31, 2024. Management based its assessment on criteria established in Internal Control - Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission. Based on that evaluation, our management concluded that our internal control over financial reporting was effective as of December 31, 2024.

This 10-K does not include an attestation report of our independent registered public accounting firm due to an exemption established by the JOBS Act for "emerging growth companies."

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) that occurred during the quarter ended December 31, 2024 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information.***Director and Executive Officer Trading Arrangements***

During the fourth quarter of 2024, none of our directors or officers adopted or terminated any contract, instruction or written plan for the purchase or sale of our securities intended to satisfy the affirmative defense conditions of Rule 10b5-1(c) under the Exchange Act or any “non-Rule 10b5-1 trading arrangement” (as defined in Item 408(c) of Regulation S-K).

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

Not Applicable.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

The information required under this item is incorporated herein by reference to our definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the SEC not later than 120 days after the close of our fiscal year ended December 31, 2024.

Item 11. Executive Compensation.

The information required under this item is incorporated herein by reference to our definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the SEC not later than 120 days after the close of our fiscal year ended December 31, 2024.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters.

The information required under this item is incorporated herein by reference to our definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the SEC not later than 120 days after the close of our fiscal year ended December 31, 2024.

Item 13. Certain Relationships and Related Transactions, and Director Independence.

The information required under this item is incorporated herein by reference to our definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the SEC not later than 120 days after the close of our fiscal year ended December 31, 2024.

Item 14. Principal Accounting Fees and Services.

The information required under this item is incorporated herein by reference to our definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the SEC not later than 120 days after the close of our fiscal year ended December 31, 2024.

PART IV

Item 15. Exhibits, Financial Statement Schedules.

- (1) For a list of the financial statements included herein, see Index to the Consolidated Financial Statements on page F-1 of this 10-K, incorporated into this Item by reference.
- (2) Financial statement schedules have been omitted because they are either not required or not applicable or the information is included in the consolidated financial statements or the notes thereto.
- (3) Exhibits:

Exhibit Number	Description
3.1***	Third Amended and Restated Certificate of Incorporation (Incorporated by reference to Exhibit 3.1 to the Company's Quarterly Report on Form 10-Q filed on June 16, 2022 (File No. 001-41374)).
3.2***	Certificate of Correction to Third Amended and Restated Certificate of Incorporation (Incorporated by reference to Exhibit 3.2 to the Company's Quarterly Report on Form 10-Q filed on November 10, 2022 (File No. 001-41374)).
3.3***	Certificate of Amendment to the Third Amended and Restated Certificate of Incorporation of PepGen Inc. (Incorporated by reference to Exhibit 3.1 to the Company's Current Report on Form 8-K filed on June 20, 2024 (File No. 001-41374)).
3.4***	Second Amended and Restated By-laws (Incorporated by reference to Exhibit 3.1 to the Company's Current Report on Form 8-K filed on March 15, 2024 (File No. 001-41374)).
4.1***	Amended and Restated Investors' Rights Agreement, dated July 30, 2021, among the Company and certain of its stockholders (Incorporated by reference to Exhibit 4.1 to the Company's Registration Statement on Form S-1, as amended (File No. 333-264335)).
4.2***	Specimen Common Stock Certificate (Incorporated by reference to Exhibit 4.2 to the Company's Registration Statement on Form S-1, as amended (File No. 333-264335)).
4.3***	Description of Securities (Incorporated by reference to Exhibit 4.3 to the Company's Annual Report on Form 10-K filed on March 23, 2023 (File No. 001-41374)).
10.1***	2020 Stock Plan, as amended, and forms of award agreements thereunder (Incorporated by reference to Exhibit 10.1 to the Company's Registration Statement on Form S-1, as amended (File No. 333-264335)).
10.2***	2022 Stock Option and Incentive Plan, and forms of award agreements thereunder (Incorporated by reference to Exhibit 10.2 to the Company's Registration Statement on Form S-1, as amended (File No. 333-264335)).
10.3***	2022 Employee Stock Purchase Plan (Incorporated by reference to Exhibit 10.3 to the Company's Registration Statement on Form S-1, as amended (File No. 333-264335)).
10.4***	Senior Executive Cash Incentive Bonus Plan (Incorporated by reference to Exhibit 10.4 to the Company's Registration Statement on Form S-1, as amended (File No. 333-264335)).
10.5***	Non-Employee Director Compensation Policy, as amended on June 20, 2024 (Incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q filed on August 8, 2024 (File No. 001-41374)).
10.6***	Form of Indemnification Agreement between the Company and each of its directors and executive officers (Incorporated by reference to Exhibit 10.5 to the Company's Registration Statement on Form S-1, as amended (File No. 333-264335)).
10.7***	Employment Agreement, dated March 21, 2023, between James McArthur and the Company (Incorporated by reference to Exhibit 10.7 to the Company's Annual Report on Form 10-K filed on March 23, 2023 (File No. 001-41374)).
10.8***	Employment Agreement, dated March 21, 2023, between Noel Donnelly and the Company (Incorporated by reference to Exhibit 10.8 to the Company's Annual Report on Form 10-K filed on March 23, 2023 (File No. 001-41374)).
10.9†***	License of Technology, dated November 23, 2020, among Oxford University Limited, Medical Research Counsel as part of the United Kingdom Research and Innovation and PepGen Limited (Incorporated by reference to Exhibit 10.10 to the Company's Registration Statement on Form S-1, as amended (File No. 333-264335)).
10.10***	Lease, dated December 1, 2021, between B9 LS Harrison & Washington LLC and the Company (Incorporated by reference to Exhibit 10.11 to the Company's Registration Statement on Form S-1, as amended (File No. 333-264335)).
10.11***	First Lease Amendment, dated January 14, 2022, between B9 LS Harrison & Washington LLC and the Company (Incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q filed on May 11, 2023 (File No. 001-41374)).
10.12***	Lease Amendment, dated March 29, 2023, between B9 LS Harrison & Washington LLC and the Company (Incorporated by reference to Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q filed on May 11, 2023 (File No. 001-41374)).
10.13***	Amendment No. 1 to the License of Technology Agreement, dated February 12, 2021, by and among Oxford University Innovation Limited, Medical Research Counsel as part of the United Kingdom Research and Innovation and PepGen Limited (Incorporated by reference to Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q filed on August 8, 2023 (File No. 001-41374)).
10.14***	Agreement for Contract Novation, dated January 1, 2022, by and among Oxford University Innovation Limited, United Kingdom Research and Innovation, PepGen Limited and PepGen Inc. (Incorporated by reference to Exhibit 10.3 to the Company's Quarterly Report on Form 10-Q filed on August 8, 2023 (File No. 001-41374)).

10.15***	At-the-Market Equity Offering Sales Agreement, dated August 8, 2023, between Stifel, Nicolaus & Company, Incorporated and the Company (Incorporated by reference to Exhibit 1.1 to the Company's Current Report on Form 8-K filed on August 8, 2023 (File No. 001-41374)).
10.16***	Employment Agreement, dated December 6, 2023, between Mary Beth DeLena and the Company. (Incorporated by reference to Exhibit 10.19 to the Company's Annual Report on Form 10-K filed on March 29, 2024 (File No. 001-41374)).
10.17***	PepGen Inc. 2024 Inducement Plan and forms of agreements thereunder (Incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q filed on November 7, 2024 (File No. 001-41374)).
10.18***	Employment Agreement, dated August 19, 2024, between Paul D. Streck, MD, MBA and the Company (Incorporated by reference to Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q filed on November 7, 2024 (File No. 001-41374)).
19.1*	PepGen Inc. Insider Trading Policy
21.1*	Subsidiaries of Registrant
23.1*	Consent of KPMG, LLP, independent registered public accounting firm.
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***	Compensation Recovery Policy (Incorporated by reference to Exhibit 97 to the Company's Annual Report on Form 10-K filed on March 29, 2024 (File No. 001-41374))
101.INS	Inline XBRL Instance Document – the instance document does not appear in the Interactive Data File because XBRL tags are embedded within the Inline XBRL document.
101.SCH	Inline XBRL Taxonomy Extension Schema Document
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

* Filed herewith.

** Furnished herewith.

*** Previously filed.

† Portions of this exhibit (indicated by asterisks) have been omitted in accordance with the rules of the SEC.

Item 16. Form 10-K Summary.

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended, the Registrant has duly caused this Report to be signed on its behalf by the undersigned, thereunto duly authorized, on February 24, 2025.

PEPGEN INC.

By: /s/ James McArthur
Name: **James McArthur**
Title: **Chief Executive Officer**

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, this Report has been signed below by the following persons on behalf of the Registrant and in the capacities indicated as of February 24, 2025.

<u>Name</u>	<u>Title</u>
<u>/s/ James McArthur</u> James McArthur, Ph. D.	Chief Executive Officer (Principal Executive Officer)
<u>/s/ Noel Donnelly</u> Noel Donnelly, M.B.A.	Chief Financial Officer (Principal Financial Officer and Principal Accounting Officer)
<u>/s/ Laurie B. Keating</u> Laurie B. Keating, J.D.	Chair of the Board of Directors
<u>/s/ Habib Joseph Dable</u> Habib Joseph Dable	Director
<u>/s/ Heidi Henson</u> Heidi Henson	Director
<u>/s/ Howard Mayer</u> Howard Mayer, M.D.	Director
<u>/s/ Joshua Resnick.</u> Joshua Resnick, M.D., M.B.A	Director

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Report of Independent Registered Public Accounting Firm

To the Stockholders and Board of Directors
PepGen Inc.:

Opinion on the Consolidated Financial Statements

We have audited the accompanying consolidated balance sheets of PepGen Inc. and subsidiaries (the Company) as of December 31, 2024 and 2023, the related consolidated statements of operations and comprehensive loss, stockholders' equity, and cash flows for each of the years in the two-year period ended December 31, 2024, and the related notes (collectively, the consolidated financial statements). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2024 and 2023, and the results of its operations and its cash flows for each of the years in the two-year period ended December 31, 2024, in conformity with U.S. generally accepted accounting principles.

Basis for Opinion

These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these consolidated 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 consolidated 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 consolidated 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 consolidated 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 consolidated financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ KPMG LLP

We have served as the Company's auditor since 2021.

Phoenix, Arizona
February 24, 2025

PEPGEN INC.
CONSOLIDATED BALANCE SHEETS
(IN THOUSANDS, EXCEPT SHARE AND PAR VALUE AMOUNTS)

	December 31,	
	2024	2023
Assets		
Current assets:		
Cash and cash equivalents	\$ 49,421	\$ 80,774
Marketable securities	70,770	29,633
Prepaid expenses and other current assets	3,570	2,271
Total current assets	\$ 123,761	\$ 112,678
Property and equipment, net	3,716	4,764
Operating lease right-of-use asset	21,432	23,620
Restricted cash	1,548	1,548
Other assets	426	442
Total assets	<u>\$ 150,883</u>	<u>\$ 143,052</u>
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	\$ 1,752	\$ 1,005
Accrued expenses	11,850	13,522
Operating lease liability	3,094	3,004
Total current liabilities	16,696	17,531
Operating lease liability, net of current portion	15,567	17,100
Total liabilities	<u>32,263</u>	<u>34,631</u>
Stockholders' equity:		
Preferred stock, \$0.0001 par value; 10,000,000 shares authorized at December 31, 2024 and 2023, respectively	—	—
Common stock, \$0.0001 par value; 500,000,000 shares authorized as of December 31, 2024 and 2023, respectively; 32,619,663 and 23,823,241 shares issued and outstanding as of December 31, 2024 and 2023, respectively	3	2
Additional paid-in capital	390,057	289,867
Accumulated other comprehensive income	23	34
Accumulated deficit	(271,463)	(181,482)
Total stockholders' equity	118,620	108,421
Total liabilities and stockholders' equity	<u>\$ 150,883</u>	<u>\$ 143,052</u>

See accompanying notes to consolidated financial statements.

PEPGEN INC.
CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS
(IN THOUSANDS, EXCEPT SHARE AND PER SHARE AMOUNTS)

	Year Ended December 31,	
	2024	2023
Operating expenses:		
Research and development	\$ 76,478	\$ 68,126
General and administrative	21,261	16,640
Total operating expenses	\$ 97,739	\$ 84,766
Operating loss	\$ (97,739)	\$ (84,766)
Other income (expense)		
Interest income	7,142	6,400
Other (expense) income, net	(1)	(187)
Total other income, net	7,141	6,213
Net loss before income tax	\$ (90,598)	\$ (78,553)
Income tax benefit (expense)	617	(73)
Net loss	\$ (89,981)	\$ (78,626)
Net loss per share, basic and diluted	\$ (2.85)	\$ (3.30)
Weighted-average common shares outstanding, basic and diluted	31,583,073	23,796,000
Other comprehensive (loss) income:		
Cumulative translation adjustment arising during the period	(50)	104
Unrealized gain on marketable securities	39	11
Comprehensive loss	\$ (89,992)	\$ (78,511)

See accompanying notes to consolidated financial statements.

PEPGEN INC.
CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY
(IN THOUSANDS, EXCEPT SHARE AMOUNTS)

	Common Stock		Additional Paid-in Capital		Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount					
Balance as of December 31, 2022	23,713,196	\$	282,566	\$	(81)	\$	179,631
Issuance of stock under the employee stock purchase plan	9,694		40		—		40
Exercise of stock options	100,351		213		—		213
Stock-based compensation expense	—		7,048		—		7,048
Unrealized gain on marketable securities	—		—		11		11
Cumulative translation adjustment arising during the period	—		—		104		104
Net loss	—		—		—	(78,626)	(78,626)
Balance as of December 31, 2023	23,823,241	\$	289,867	\$	34	\$	108,421
Issuance of stock in public offering, net of underwriters' fees and issuance costs of \$3,730	7,530,000		76,351		—		76,352
Issuance of common stock from At-the-Market Sales Agreement, net of underwriters' fees of \$100	1,000,000		9,900		—		9,900
Issuance of stock under the employee stock purchase plan	56,540		252		—		252
Exercise of stock options	209,882		2,230		—		2,230
Stock-based compensation expense	—		11,457		—		11,457
Unrealized gain on marketable securities	—		—		39		39
Cumulative translation adjustment arising during the period	—		—		(50)		(50)
Net loss	—		—		—	(89,981)	(89,981)
Balance as of December 31, 2024	32,619,663	\$	390,057	\$	23	\$	118,620

See accompanying notes to consolidated financial statements.

PEPGEN INC.
CONSOLIDATED STATEMENTS OF CASH FLOWS
(IN THOUSANDS)

	Year Ended December 31,	
	2024	2023
Cash flows from operating activities:		
Net loss	\$ (89,981)	\$ (78,626)
Adjustments to reconcile net loss to cash used in operating activities:		
Depreciation	1,505	1,184
Stock-based compensation expense	11,457	7,048
Amortization and interest accretion related to operating lease	3,748	(334)
Amortization and accretion of premium and discounts on marketable securities, net	(3,925)	(220)
Other non-cash adjustments	70	—
Changes in operating assets and liabilities:		
Prepays and other current and non-current assets	(1,301)	2,064
Accounts payable	722	(369)
Accrued expenses and other non-current liabilities	(1,663)	1,422
Operating lease liabilities, current and non-current	(3,004)	(1,166)
Net cash used in operating activities	(82,372)	(68,997)
Cash flows from investing activities:		
Purchases of property and equipment	(497)	(2,599)
Purchases of marketable securities	(145,171)	(29,404)
Maturities of marketable securities	108,000	—
Net cash used in investing activities	(37,668)	(32,003)
Cash flows from financing activities:		
Issuance of common stock upon initial public offering, net of underwriters' fees	76,878	—
Payment of offering costs	(511)	(442)
Issuance of common stock from At-the-Market Sales Agreement, net of underwriters' fees	9,900	—
Proceeds from employee equity plans	2,482	253
Net cash provided by (used in) financing activities	88,749	(189)
Effect of exchange rate changes on cash	(62)	286
Net (decrease) in cash, cash equivalents and restricted cash	\$ (31,353)	\$ (100,903)
Cash, cash equivalents and restricted cash at beginning of period	82,322	183,225
Cash, cash equivalents and restricted cash at end of period	<u>\$ 50,969</u>	<u>\$ 82,322</u>
Components of cash, cash equivalents and restricted cash		
Cash and cash equivalents	\$ 49,421	\$ 80,774
Restricted cash	1,548	1,548
Total cash, cash equivalents and restricted cash at end of period	<u>\$ 50,969</u>	<u>\$ 82,322</u>
Supplemental noncash investing and financing activities		
Property and equipment included in accounts payable and accrued expenses	\$ 31	\$ 14
Cash paid for taxes	71	2,702

See accompanying notes to consolidated financial statements.

PEPGEN INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

1. Nature of Business and Basis of Presentation

PepGen Inc., hereinafter referred to as PepGen or the Company, is a clinical-stage biotechnology company advancing the next generation of oligonucleotide therapeutics with the goal of transforming the treatment of severe neuromuscular and neurologic diseases. The Company's principal offices are located in Boston, Massachusetts.

The Company was initially formed as PepGen Limited on January 25, 2018, in the United Kingdom, or the U.K. On November 9, 2020, PepGen Limited completed a corporate reorganization, or the Reorganization. As part of the Reorganization, PepGen Limited formed PepGen, a Delaware corporation with nominal assets and liabilities, for the purpose of consummating the Reorganization. In connection with the Reorganization, the existing stockholders of PepGen Limited exchanged each of its classes of shares of PepGen Limited for the same number and class of common stock of PepGen on a one-to-one basis. The newly issued stock of PepGen had substantially identical rights to the exchanged shares of PepGen Limited. As a result of the exchange, PepGen became the sole stockholder of PepGen Limited. Upon the completion of the Reorganization on November 23, 2020, the historical financial statements of PepGen Limited became the historical financial statements of PepGen as the Reorganization was deemed to be between entities under common control. PepGen Limited was dissolved on December 10, 2024.

Liquidity and Going Concern

Since inception, the Company has not generated any revenue from product sales or other sources and has incurred significant operating losses and negative cash flows from operations. The Company's primary uses of cash, cash equivalents, and marketable securities to date have been funding research and development activities, business planning, establishing and maintaining the Company's intellectual property portfolio, hiring personnel, leasing premises and associated capital expenditures, raising capital, and providing general and administrative support for these operations. As of December 31, 2024, the Company had an accumulated deficit of \$271.5 million. To date, the Company has funded operations primarily through private placements of convertible preferred stock, the sale of shares of common stock in its initial public offering, or IPO, the sale of shares of common stock under its At-the-Market Equity Offering Sales Agreement, or Sales Agreement, with Stifel, Nicolaus & Company, Incorporated, or Stifel, and through the sale of shares of common stock in a follow-on public offering, referred to as the Follow-on Offering. As of December 31, 2024, the Company had cash, cash equivalents, and marketable securities of \$120.2 million. The Company believes that its cash, cash equivalents, and marketable securities as of December 31, 2024, will be sufficient to fund its currently planned operations for at least the next 12 months from the issuance of these consolidated financial statements.

The Company filed a shelf registration statement on Form S-3 with the United States Securities and Exchange Commission, or SEC, which covers the offering, issuance and sale of an amount up to \$300.0 million in the aggregate of shares of common stock, preferred stock, debt securities, warrants, and/or units or any combination thereof, which was declared effective on June 16, 2023. On August 8, 2023, the Company filed a prospectus supplement and entered into the Sales Agreement with Stifel, as sales agent, which provides for the issuance and sale by the Company of up to \$100.0 million of shares of common stock from time to time in "at-the-market" offerings. The sales agent is entitled to receive a commission of up to 3.0% of gross proceeds from sales under the Sales Agreement. On February 5, 2024, the Company sold 1,000,000 shares of common stock at a price of \$10.00 per share under the Sales Agreement, resulting in net proceeds of \$9.9 million. On February 9, 2024, the Company sold 7,530,000 shares of common stock in the Follow-on Offering, pursuant to an underwriting agreement with Leerink Partners LLC dated as of February 6, 2024, at a price of \$10.635 per share, resulting in net proceeds of \$76.4 million after deducting underwriting fees and offering costs of \$3.7 million. Net proceeds from sales under the Sales Agreement and Follow-on Offering, after deducting underwriters' fees and costs, were \$86.3 million. On June 28, 2024, the Company filed a second shelf registration statement on Form S-3 with the SEC, which covers the offering, issuance and sale of an amount up to \$250.0 million in the aggregate of shares of common stock, preferred stock, debt securities, warrants, and/or units or any combination thereof, which was declared effective on July 8, 2024.

As the Company continues to pursue its business plan to successfully develop and obtain regulatory approval for its product candidates, it expects to finance its operations through the sale of equity, debt financings or other capital resources, which could include income from collaborations, strategic partnerships or marketing, distribution, licensing or other strategic arrangements with third parties, or from grants. However, there can be no assurance that any additional financing or strategic transactions will be available to the Company on acceptable terms, if at all. If events or circumstances occur such that the Company does not obtain additional funding, it may need to delay, reduce or eliminate its product development or future commercialization efforts, which could have a material adverse effect on the Company's business, results of operations or financial condition.

Basis of Presentation and Consolidation

The accompanying consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States, or U.S. GAAP. The consolidated financial statements include the accounts of PepGen Inc. (a U.S. corporation) and its wholly owned subsidiaries PepGen Limited (a U.K. corporation which was dissolved on December 10, 2024) and PepGen Securities Corp. (a U.S. corporation). All intercompany accounts and transactions have been eliminated in consolidation.

Reclassifications

Restricted cash on the consolidated balance sheet as of December 31, 2023, previously included in other assets, has been presented as a separate line item. The consolidated financial statements have otherwise been prepared on the same basis as the audited 2023 consolidated financial statements. The reclassification has no effect on net income, earnings per share, retained earnings, cash flows or total assets.

2. Summary of Significant Accounting Policies

Use of Estimates

The preparation of consolidated financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the amounts reported in the consolidated financial statements and accompanying notes. Management bases its estimates and judgments on historical experience, knowledge of current conditions, and beliefs of what could occur in the future, given the available information. On an ongoing basis, management evaluates such estimates and assumptions for continued reasonableness. In particular, management makes estimates with respect to accruals for research and development activities, for the valuation of intellectual property, for the fair value of common stock and convertible preferred stock warrants and stock-based compensation expense. Appropriate adjustments, if any, to the estimates used are made prospectively based upon such periodic evaluation. Actual results could differ materially from those estimates and assumptions.

Segment Reporting

Operating segments are identified as components of an enterprise about which separate discrete financial information is available for evaluation by the chief operating decision-maker, or CODM. The Company's CODM is its chief executive officer who reviews financial information together with certain operating metrics principally to make decisions about how to allocate resources and to measure the Company's performance. The Company has determined that it operates as a single reportable segment. The Company's CODM evaluates financial information on a consolidated basis.

Foreign Currency Remeasurement

The Company's reporting currency is the U.S. Dollar. The functional currency of PepGen Limited is the British Pound. The assets and liabilities of PepGen Limited are translated into U.S. Dollars at the exchange rates in effect at each balance sheet date, and the results of operations are translated using the average exchange rates prevailing throughout the reporting period. Adjustments resulting from translating foreign functional currency financial statements into U.S. Dollars are included in the cumulative translation adjustment, a component of accumulated other comprehensive loss in stockholders' equity.

Concentration of Credit Risk

Financial instruments, which potentially subject the Company to concentrations of credit risk, consist of cash and money market accounts. As of December 31, 2024, the Company's cash, cash equivalents, and marketable securities were held by four financial institutions in the U.S. At times, the Company's deposits held in the U.S. may exceed the respective insured limits of the Federal Depository Insurance Corporation and Financial Services Compensation Scheme.

Cash and Cash Equivalents

The Company considers all highly liquid investments with an original maturity of three months or less when purchased to be cash equivalents. Cash and cash equivalents are recorded at cost, which approximates fair value. As of December 31, 2024 and 2023, cash and cash equivalents consisted primarily of checking and money market funds composed of U.S. government obligations, and U.S. treasury notes.

Restricted Cash

The Company classifies all cash the use of which is limited by contractual provisions as restricted cash. Restricted cash arises from the requirement for the Company to maintain cash of \$1.5 million as collateral under a lease agreement.

Marketable Securities

The Company's marketable securities consist of U.S. treasury notes which are classified as available-for-sale and are reported at fair value. Unrealized gains and losses on available-for-sale debt securities are reported as a component of accumulated other comprehensive loss in stockholders' equity. Realized gains and losses are based on the specific identification method and are included as a component of other income (expense), net in the consolidated statements of operations and comprehensive loss.

The Company evaluates its marketable securities with unrealized losses for other-than-temporary impairment. When assessing marketable securities for other-than-temporary declines in value, the Company considers such factors as, among other things, how significant the decline in value is as a percentage of the original cost, how long the market value of the investment has been less than its original cost, the Company's ability and intent to retain the investment for a period of time sufficient to allow for any anticipated recovery in fair value, and market conditions in general. If any adjustment to fair value reflects a decline in the value of the investment that the Company considers to be "other-than-temporary," the Company reduces the investment to fair value through a charge to the consolidated statement of operations and comprehensive loss. No such adjustments were necessary during the periods presented.

Fair Value Measurements

Certain assets and liabilities of the Company are carried at fair value under U.S. GAAP. Fair value is defined as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. Valuation techniques used to measure fair value must maximize the use of observable inputs and minimize the use of unobservable inputs. Financial assets and liabilities carried at fair value are to be classified and disclosed in one of the following three levels of the fair value hierarchy, of which the first two are considered observable and the last is considered unobservable:

- Level 1: Fair values are determined utilizing prices (unadjusted) in active markets for identical assets or liabilities that the Company has the ability to access.
- Level 2: Observable inputs (other than Level 1 quoted prices), such as quoted prices in active markets for similar assets or liabilities, quoted prices in markets that are not active for identical or similar assets or liabilities, or other inputs that are observable or can be corroborated by observable market data.
- Level 3: Unobservable inputs that are supported by little or no market activity that are significant to determining the fair value of the assets or liabilities, including pricing models, discounted cash flow methodologies and similar techniques.

For certain financial instruments, including cash and cash equivalents, prepaid expenses, accounts payable, as well as certain accrued liabilities, the recorded amount approximates estimated fair value due to their relatively short maturity period.

Property and Equipment, Net

Property and equipment are stated at cost, net of accumulated depreciation. Depreciation of property and equipment is calculated using the straight-line method over the estimated useful lives of the respective assets. Maintenance and repairs that do not improve or extend the life of the assets are expensed when incurred.

The estimated useful lives of the Company's property and equipment are as follows:

Laboratory and computer equipment	5 years
Furniture and fixtures	3 years

Deferred Offering Costs

The Company capitalizes within other long-term assets certain legal, accounting, and other third-party fees that are directly related to the Company's in-process equity financings, until such financings are consummated. After consummation of the equity financing, these costs are recorded as a reduction of the proceeds received as a result of the offering. Should a planned equity financing be abandoned, terminated, or significantly delayed, the deferred offering costs are immediately written off to operating expenses. As of December 31, 2024, deferred offering costs of \$0.4 million in relation to the Company's shelf registration statements on Form S-3 were recorded within other assets on the consolidated balance sheets.

Leases

Under ASU 2016-02, *Leases (Topic 842)*, or ASC 842, at the inception of an arrangement, the Company determines whether the arrangement is or contains a lease based on the unique facts and circumstances presented in the arrangement, including whether the Company controls the use of identified assets. The Company classifies leases with a term greater than one year as either operating or finance leases at the lease commencement date and records a right-of-use asset and current and non-current lease liabilities, as applicable on the balance sheet. The Company has elected not to recognize on the balance sheet leases with terms of one year or less, but payments are recognized as expense on a straight-line basis over the lease term. If a lease includes options to extend the lease term, the Company does not assume the option will be exercised in its initial lease term assessment unless there is reasonable certainty that the Company will renew based on an assessment of economic factors present as of the lease commencement date. The Company monitors its plans to renew its material lease each reporting period. If a lease includes provisions for leasehold improvements for which the Company has an obligation to pay, the Company determines if the improvements should be considered lessor or lessee assets. If the improvements are considered lessor assets, the Company records the payments in the calculation of the lease liability and corresponding right-of-use asset.

Lease liabilities and the corresponding right-of-use assets are recorded based on the present value of lease payments over the remaining lease term. The present value of future lease payments are discounted using the interest rate implicit in lease contracts if that rate is readily determinable; otherwise, the Company utilizes information available at the commencement of the lease to calculate the incremental borrowing rate, or IBR, which reflects the fixed rate at which the Company could borrow on a collateralized basis over a similar term, the amount of the lease payments in a similar economic environment. In order to determine the appropriate IBR, the Company uses available third-party information, including comparable company collateralized borrowing information. After lease commencement and the establishment of a right-to-use asset and operating lease liability, lease expense is recorded on a straight-line basis over the lease term.

The Company enters into contracts that contain both lease and non-lease components. Non-lease components include costs that do not provide a right-to-use leased asset but instead provide a service, such as maintenance costs. The Company has elected to account for the lease and non-lease components together as a single component for all classes of underlying assets. Variable costs associated with the lease, such as maintenance and utilities, are not included in the measurement of right-to-use assets and lease liabilities but rather are expensed when the events determining the amount of variable consideration to be paid have occurred.

Impairment of Long-Lived Assets

The Company reviews long-lived assets for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset or asset group may not be recoverable. The recoverability of assets to be held and used is measured by a comparison of the carrying amount of an asset or asset group to the estimated undiscounted future cash flows expected to be generated by the asset or asset group.

If the carrying amount of an asset or asset group exceeds its estimated undiscounted future cash flows, an impairment charge is recognized as the amount by which the carrying amount of the asset or asset group exceeds the estimated discounted future cash flows of the asset or asset group. There have been no such impairments of long-lived assets for the years ended December 31, 2024 and 2023.

Commitment and Contingencies

The Company recognizes a liability with regard to loss contingencies when it believes it is probable a liability has been incurred, and the amount can be reasonably estimated. If some amount within a range of loss appears at the time to be a better estimate than any other amount within the range, the Company accrues that amount. When no amount within the range is a better estimate than any other amount, the Company accrues the minimum amount in the range. The Company has not recorded any such liabilities as of December 31, 2024 and 2023 that were material to the consolidated financial statements.

Research and Development

Research and development costs are expensed as incurred. Research and development costs consist of salaries, benefits, and other personnel-related costs, including stock-based compensation, laboratory supplies, process development costs, fees paid to other entities to conduct certain research and development activities on the Company's behalf, including contract manufacturing organizations and contract research organizations, and allocated facility and other related costs. Non-refundable advance payments for goods or services that will be used or rendered for future research and development activities are deferred and capitalized as prepaid expenses until the related goods are delivered or services are performed. The Company has not recorded any research and development credits on the consolidated balance sheet at December 31, 2024 and 2023.

The Company records accrued liabilities for estimated costs of research and development activities conducted by third-party service providers. The Company accrues for these costs based on factors such as estimates of the work completed and in accordance

with agreements established with its third-party service providers under the service agreements. The Company makes significant judgments and estimates in determining the accrued liabilities balance in each reporting period. As actual costs become known, the Company adjusts its accrued liabilities. The historical accrual estimates made by the Company have not been materially different from the actual costs.

Stock-Based Compensation

The Company accounts for its stock-based compensation in accordance with ASC Topic 718, *Compensation-Stock Compensation*, or ASC 718. ASC 718 requires all stock-based payments to employees, non-employees and directors, to be recognized as expense in the consolidated statements of operations based on their grant date fair values. The Company estimates the fair value of stock options granted using the Black-Scholes option pricing model, or Black-Scholes, for stock option grants to employees, non-employees and directors. The fair value of the Company's common stock is used to determine the fair value of restricted stock awards.

The Company's stock-based compensation awards are generally subject to service-based vesting conditions. Compensation expense related to awards to employees, non-employees and directors with service-based vesting conditions is recognized on a straight-line basis based on the grant date fair value over the associated service period of the award, which is generally the vesting term.

Black-Scholes requires inputs based on certain subjective assumptions, including (i) the expected stock price volatility, (ii) the expected term of the award, (iii) the risk-free interest rate and (iv) expected dividends. The Company determines the expected volatility using the historical volatility of a peer group of comparable publicly traded companies with product candidates in similar stages of development to the Company's product candidates. The Company uses the simplified method as prescribed by the SEC Staff Accounting Bulletin No. 107, *Share-Based Payment*, to calculate the expected term for stock options granted to employees, non-employees and directors whereby, the expected term equals the arithmetic average of the vesting term and the original contractual term of the stock options due to its lack of sufficient historical data. The risk-free interest rate is based on U.S. Treasury securities with a maturity date commensurate with the expected term of the associated award. The expected dividend yield is assumed to be zero as the Company has never paid dividends and has no current plans to pay any dividends on its common stock. The Company recognizes forfeitures as they occur.

The fair value of the common stock underlying stock-based awards is the closing price of the Company's common stock on the date of grant.

The Company classifies stock-based compensation expense in its consolidated statements of operations in the same manner in which the award recipient's payroll costs are classified or in which the award recipient's service payments are classified.

Income Taxes

Income taxes are accounted for using the asset and liability method. Deferred tax assets and liabilities are recognized for the future tax consequences attributable to differences between the financial statement carrying amounts or existing assets and liabilities and their respective tax bases. Deferred tax assets and liabilities are measured using the enacted tax rates expected to apply to taxable income in the years in which those temporary differences are expected to be recovered or settled. The effect on deferred tax assets and liabilities of a change in tax rates is recognized in income in the period of enactment. The Company records a valuation allowance to reduce deferred tax assets to an amount for which realization is more likely than not.

The Company recognizes the tax benefit from an uncertain tax position if it is more likely than not that the tax position will be sustained upon examination by the tax authorities, based on the merits of the position. The Company's policy is to recognize interest and penalties related to the underpayment of income taxes as a component of income tax expense or benefit. To date, there have been no interest or penalties charged in relation to the unrecognized tax benefits.

Comprehensive Loss

Comprehensive loss is composed of two components — net loss and other comprehensive loss. Other comprehensive loss refers to gains and losses that under U.S. GAAP are recorded as an element of stockholders' equity but are excluded from net loss. The Company's other comprehensive loss consists of foreign currency translation adjustments and unrealized gains and losses on available-for-sale marketable debt securities.

Net Loss Per Share

Basic net loss per share is calculated by dividing the net loss attributable to common stockholders by the weighted average number of shares of common stock outstanding for the period, without consideration of potential dilutive securities. Diluted net loss per share is computed by dividing the net loss attributable to common stockholders by the sum of the weighted average number of common shares plus the potential dilutive effects of potential dilutive securities outstanding during the period.

Potential dilutive securities are excluded from diluted earnings or loss per share if the effect of such inclusion is anti-dilutive. The Company's potentially dilutive securities include unvested common stock under the Company's equity incentive plan which have been excluded from the computation of diluted net loss per share as they would be anti-dilutive to the net loss per share. For all periods presented, there is no difference in the number of shares used to calculate basic and diluted shares outstanding due to the Company's net loss position.

The following table sets forth the outstanding potentially dilutive securities that have been excluded in the calculation of diluted net loss per share because their inclusion would be anti-dilutive:

	As of December 31,	
	2024	2023
Options to purchase common stock	5,845,039	4,233,203
Total	5,845,039	4,233,203

Emerging Growth Company Status

The Company is an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012, or JOBS Act, and may take advantage of certain exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies. The Company may take advantage of these exemptions until the Company is no longer an "emerging growth company." Section 107 of the JOBS Act provides that an "emerging growth company" can take advantage of the extended transition period afforded by the JOBS Act for the implementation of new or revised accounting standards. The Company has elected to use the extended transition period for complying with new or revised accounting standards and as a result of this election, its consolidated financial statements may not be comparable to companies that comply with public company effective dates. The Company may take advantage of these exemptions up until the last day of the fiscal year following the fifth anniversary of the IPO or such earlier time that it is no longer an "emerging growth company." As a result of the Company having elected the extended transition period for complying with new or revised accounting standards pursuant to Section 107(b) of the JOBS Act, 2016-13 and ASU 2019-11 are effective for the Company for fiscal years beginning after December 15, 2022, and interim periods within those fiscal years.

Recent Accounting Pronouncements

From time to time, new accounting pronouncements are issued by the Financial Accounting Standards Board, or FASB, or other standard-setting bodies that the Company adopts as of the specified effective date. The Company qualifies as an "emerging growth company" as defined in the JOBS Act and has elected not to "opt out" of the extended transition related to complying with new or revised accounting standards, which means that when a standard is issued or revised and it has different application dates for public and non-public companies, the Company can adopt the new or revised standard at the time non-public companies adopt the new or revised standard and can do so until such time that the Company either (i) irrevocably elects to "opt out" of such extended transition period or (ii) no longer qualifies as an emerging growth company. The Company may choose to early adopt any new or revised accounting standards whenever such early adoption is permitted for non-public companies. Unless otherwise discussed, the Company believes that the impact of recently issued standards that are not yet effective will not have a material impact on its consolidated financial statements and disclosures.

In November 2023, the FASB issued ASU No. 2023-07, *Segment Reporting (Topic 280)*, or ASU 2023-07. This update expands segment disclosure requirements, including new segment disclosure requirements for entities with a single reportable segment among other disclosure requirements. This update is effective for the Company in the consolidated financial statements for the year ending December 31, 2024, and interim periods beginning on January 1, 2025. The Company adopted this standard for the year ended December 31, 2024. (See Note 12 - Segment Reporting).

In December 2023, the FASB issued ASU No. 2023-09, *Income Taxes (Topic 740): Improvement to Income Tax Disclosures*, or ASU 2023-09, to enhance the transparency and decision usefulness of income tax disclosures. ASU 2023-09 is effective for annual periods beginning after December 15, 2024 on a prospective basis. Early adoption and retrospective application is permitted. The Company is currently evaluating the potential impact of the adoption of ASU 2023-09 on its consolidated financial statements and related disclosures.

In November 2024, the FASB issued ASU No. 2024-03, *Income Statement—Reporting Comprehensive Income—Expense Disaggregation Disclosures (Subtopic 220-40)*, or ASU 2024-03. ASU 2024-03 requires companies to disaggregate certain expenses presented on the face of the financial statements to enhance transparency and help investors better understand an entity's performance within the notes to the financial statements. The amendments in ASU 2024-03 are effective for fiscal years beginning after December 15, 2026, and interim periods within fiscal years beginning after December 15, 2027, with early adoption permitted. The Company will not be required to adopt ASU 2024-03 until January 1, 2027. The Company is currently evaluating the potential impact of the adoption of ASU 2024-03 on its consolidated financial statements and related disclosures.

3. Fair Value Measurements

The following tables present information about the Company's financial assets that have been measured at fair value as of December 31, 2024 and December 31, 2023, and indicate the fair value of the hierarchy of the valuation inputs utilized to determine such fair value. In general, fair values determined by Level 1 inputs utilize quoted prices (unadjusted) in active markets for identical assets or liabilities. Fair value determined by Level 2 inputs utilize observable inputs other than Level 1 prices, such as quoted prices for similar assets or liabilities, quoted market prices in markets that are not active or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the related assets or liabilities. Fair values determined by Level 3 inputs are unobservable data points for the asset or liability, and include situations where there is little, if any, market activity for the asset or liability. The following tables set forth marketable securities as of December 31, 2024 and December 31, 2023 (in thousands):

	As of December 31, 2024			
	Amortized Cost	Unrealized Gains	Unrealized Losses	Total
U.S. Treasury-backed money market funds	70,731	61	(22)	70,770
Total	<u>\$ 70,731</u>	<u>\$ 61</u>	<u>\$ (22)</u>	<u>\$ 70,770</u>

	As of December 31, 2023			
	Amortized Cost	Unrealized Gains	Unrealized Losses	Total
U.S. Treasury-backed money market funds	29,622	11	—	29,633
Total	<u>\$ 29,622</u>	<u>\$ 11</u>	<u>\$ —</u>	<u>\$ 29,633</u>

The following tables set forth the fair value of the Company's financial assets measured at fair value on a recurring basis and indicate the level within the fair value hierarchy utilized to determine such values (in thousands):

	As of December 31, 2024			
	Total	Level 1	Level 2	Level 3
Cash Equivalents:				
U.S. Treasury-backed money market funds	\$ 45,570	\$ 45,570	\$ —	\$ —
U.S. Treasury notes	—	—	—	—
Marketable Securities:				
U.S. Treasury notes	\$ 70,770	\$ 70,770	\$ —	\$ —
Total	<u>\$ 116,340</u>	<u>\$ 116,340</u>	<u>\$ —</u>	<u>\$ —</u>

	As of December 31, 2023			
	Total	Level 1	Level 2	Level 3
Cash Equivalents:				
U.S. Treasury-backed money market funds	\$ 64,397	\$ 64,397	\$ —	\$ —
U.S. Treasury notes	11,980	11,980	—	—
Marketable Securities:				
U.S. Treasury notes	\$ 29,633	\$ 29,633	\$ —	\$ —
Total	<u>\$ 106,010</u>	<u>\$ 106,010</u>	<u>\$ —</u>	<u>\$ —</u>

Money market funds are highly liquid investments that are valued based on quoted market prices in active markets, which represent a Level 1 measurement within the fair value hierarchy. These money market funds are classified on the consolidated balance sheets under cash and cash equivalents.

4. Property and Equipment, Net

The cost and accumulated depreciation of property and equipment were as follows (in thousands):

	December 31,	
	2024	2023
Lab equipment	\$ 5,110	\$ 4,821
Computer and office equipment	1,556	1,446
Construction in process	96	69
Total property and equipment	6,762	6,336
Less accumulated depreciation	(3,046)	(1,572)
Total property and equipment, net	<u>\$ 3,716</u>	<u>\$ 4,764</u>

Depreciation expense was \$1.5 million and \$1.2 million for the years ended December 31, 2024 and 2023, respectively.

5. Accrued Expenses

Accrued expenses consisted of the following (in thousands):

	December 31,	
	2024	2023
Research and development	\$ 6,903	\$ 9,521
Employee-related expenses	3,617	2,368
Professional services	1,138	715
Other	192	918
Total accrued expenses	<u>\$ 11,850</u>	<u>\$ 13,522</u>

6. Leases

In December 2021, the Company entered into a non-cancellable operating lease agreement, or the Harrison Lease, pursuant to which the Company leases 31,668 square feet of office and laboratory space located in Boston, Massachusetts, or the Premises. The Harrison Lease commenced for accounting purposes when the Company gained access to the Premises on December 29, 2022, or the Lease Commencement Date. The Harrison Lease has a term of nine years and two months from the Lease Commencement Date. The Company's obligation for the payment of base rent for the Premises began in May 2023, and is \$0.2 million per month, increasing up to \$0.3 million per month during the term of the Lease. The Company has one option to extend the term of the Harrison Lease, for a period of an additional five years. This is not included in the lease term as it was not deemed probable that the Company would exercise this option. At December 31, 2024, the Harrison Lease was the only lease for which the Company recorded a lease liability and corresponding right-of-use asset.

The landlord completed significant leasehold improvements to the Premises, a portion of which the Company was obligated to pay per the terms of the Harrison Lease. The Company paid \$2.0 million for the improvements prior to the Lease Commencement Date, and paid \$3.4 million for the improvements in 2023, for total payments to the landlord for improvements of \$5.4 million. The Company determined that the landlord is the accounting owner of the improvements, and payments by the Company for the improvements are included in the calculation of the right-of-use asset and lease liability.

During the first quarter of 2023, the Company leased office space in Cambridge, Massachusetts, the terms of which were month-to-month, with a 30-day written notice of cancellation. The Company terminated this lease in January 2023. The Company also leased laboratory space at the University of Massachusetts, Mount Ida Campus in Newton, Massachusetts, with an initial lease term from

February 1, 2022 to January 31, 2023, which the Company extended until March 2023. All of these leases had initial terms of under 12 months and are considered short-term lease costs and are not recognized on the consolidated balance sheets.

Summary of Lease Costs

The components of lease cost under ASC 842 for the leases were as follows (in thousands):

	December 31,	
	2024	2023
Fixed lease cost	\$ 3,748	\$ 3,799
Variable lease cost	1,965	993
Short-term lease cost	—	188
Total lease cost	<u>\$ 5,713</u>	<u>\$ 4,980</u>

Supplemental disclosure of cash flow information under ASC 842 for the leases was as follows (in thousands):

	December 31, 2024
Operating cash payments for operating leases	<u>\$ 3,004</u>

Cash payments for operating leases during 2024 related to \$3.0 million in rent payments under the Harrison Lease. Additionally, the Company made payments on variable lease costs throughout the year of \$2.0 million. These payments related to parking, management fees, and other costs associated with maintaining our office and lab space.

The remaining lease term for the Harrison Lease is 7.4 years, and the discount rate is 8.0%.

Future minimum lease payments under the non-cancelable operating lease consisted of the following as of December 31, 2024:

Year Ending December 31,	(in thousands)
2025	\$ 3,094
2026	3,187
2027	3,282
2028	3,381
2029	3,483
Thereafter	8,596
Total future minimum lease payments	<u>\$ 25,023</u>
Less: imputed interest	(6,362)
Present value of lease liability	<u>\$ 18,661</u>

Included in the consolidated balance sheet (in thousands)	December 31, 2024
Lease liability	\$ 3,094
Lease liability, net of current portion	15,567
Total lease liability	<u>\$ 18,661</u>

7. Related Party Transactions

Technology License Agreement with Oxford University Innovation Limited

In March 2018, the Company, Oxford University Innovation Limited, or OUI, and the Medical Research Council of United Kingdom Research and Innovation, or MRC, or collectively, the Licensors, entered into a license of technology agreement, which was subsequently amended in December 2018, further amended and restated in November 2020, and further amended in February 2022, referred to, as so amended, as the License Agreement. The Licensors and affiliates held shares of Series A-1 and Series A-2 preferred stock, Series B preferred stock and Class A common stock. The License Agreement provides the Company with an exclusive world wide license to licensed data and technology owned by OUI and MRC in respect of cell-penetrating peptides for the treatment of Duchenne muscular dystrophy, spinal muscular atrophy, and other conditions. The License Agreement provides the Company with the rights to grant and authorize sublicenses to make, use, sell, and import products and otherwise exploit the patent rights.

As consideration for the license, the Company made an initial upfront payment in 2018, as well as a Restatement Completion Fee and a License Data Fee (each as defined in the License Agreement) in 2020 totaling \$0.1 million.

The Company could be required to make milestone payments to the Licensors upon achievement of certain patent and commercial milestones related to the patents and commercialization of certain of the Company's product candidates. The aggregate potential milestone payments are \$0.1 million. In 2024, the Company paid the Licensors a patent procurement milestone of £10,000, adjusted per the retail price index under the terms of the License Agreement. The Company also agreed to pay the Licensors low single digit royalties on net sales of any licensed products that are commercialized by the Company in excess of a threshold amount between £20 million and £30 million (\$25.1 million and \$37.7 million as of December 31, 2024), subject to certain adjustments. The term of the License Agreement continues until the later of (i) the date on which all the patents and patent applications covered thereunder have been abandoned or allowed to lapse or expired or been rejected or revoked or (ii) 20 years from the date of the original license agreement.

Upon completion of the IPO, the Company became obligated to pay OUI an exit fee between 0.5% to 2% of the value determined in an acquisition or initial public offering, not to exceed £5 million (\$6.2 million as of the IPO date). The exit fee due to OUI, based on the proceeds of the IPO, was \$1.4 million, which was paid during the second quarter of 2022 and included in research and development expense on the condensed consolidated statement of operations.

During the year ended December 31, 2024, one member of the Company's board of directors, Dr. Christopher Ashton, was employed by Oxford Science Enterprises, or OSE, which is an affiliate of OUI. On September 19, 2024, the Company announced that Dr. Ashton had resigned from the board of directors, effective as of September 30, 2024.

As of December 31, 2024, OSE owned 14.6% of the Company's outstanding common stock. Pursuant to the terms of Dr. Ashton's employment agreement with OSE, he was obligated to transfer any cash compensation from the Company to OSE. Fees paid in cash for Dr. Ashton's service on the Company's board of directors were paid directly to OSE and were included within general and administrative expense on the consolidated statement of operations. The Company paid \$36,875 and \$47,500 to OSE for the years ended December 31, 2024 and 2023, respectively, as compensation for Dr. Ashton's service on the board of directors.

RA Capital Management, L.P.

Entities affiliated with RA Capital Management, L.P., or RA Capital, purchased common stock in the Company's IPO in May 2022 and the Company's Follow-on Offering in February 2024. As of December 31, 2024, entities affiliated with RA Capital owned 32.8% of the Company's outstanding common stock.

Two members of the Company's board of directors, Dr. Joshua Resnick and Habib Dable, are affiliated with RA Capital. Pursuant to the governing legal documents of RA Capital, Dr. Resnick is obligated to transfer any cash compensation from the Company to RA Capital. Fees paid in cash for Dr. Resnick's service on the Company's board of directors were paid directly to RA Capital and are included within general and administrative expense on the consolidated statement of operations. The Company paid \$45,500 and \$43,000 to RA Capital for the years ended December 31, 2024 and 2023, respectively, for Dr. Resnick's service on the board of directors.

8. Commitments and Contingencies

Legal proceedings

From time to time, the Company may have certain contingent liabilities that arise in the ordinary course of its business activities. The Company accrues a liability for such matters when it is probable that future expenditures will be made and that such expenditures can be reasonably estimated.

The Company is not party to any litigation and does not have contingency reserves established for any litigation liabilities.

Other

The Company enters into standard indemnification agreements in the ordinary course of business. Pursuant to the agreements, the Company agrees to indemnify, hold harmless, and to reimburse the indemnified party for losses suffered or incurred by the indemnified party, including in connection with any U.S. patent or any copyright or other intellectual property infringement claim by any third-party with respect to the Company's products. Further, the Company indemnifies its directors and officers who are, or were, serving at the Company's request in such capacities. The Company's maximum exposure under these arrangements is unknown as of December 31, 2024. The Company does not anticipate recognizing any significant losses relating to these arrangements. The term of these indemnification agreements is generally perpetual any time after execution of the agreement. The maximum potential amount of future payments the Company could be required to make under these indemnification agreements may be unlimited. The Company has never incurred costs to defend lawsuits or settle claims related to these indemnification agreements.

9. Stockholders' Equity

Under the Third Amended and Restated Certificate of Incorporation, dated May 10, 2022, as amended on June 20, 2024, as currently in effect, the Company has the authority to issue a total of 500,000,000 shares of common stock (par value of \$0.0001 per share) and 10,000,000 shares of undesignated preferred stock (par value of \$0.0001 per share). Each share of common stock has the right to one vote. The holders of common stock are also entitled to receive dividends whenever funds are legally available and when declared by the board of directors, subject to the prior rights of holders of all classes of stock outstanding having priority rights as to

dividends. No cash dividends were declared by the board of directors during the years ended December 31, 2024 and December 31, 2023.

The Company has reserved shares of common stock for issuance, on an as-converted basis, as follows:

	December 31,	
	2024	2023
Stock options issued and outstanding	5,845,039	4,233,203
Unvested restricted stock and performance stock units	101,280	—
Authorized for future stock awards or option grants under the 2022 Plan	657,167	1,091,187
Authorized for future stock awards or option grants under the Inducement Plan	702,184	—
Authorized for future issuance under the ESPP	397,998	216,306
Stock options issued and outstanding	<u>7,703,668</u>	<u>5,540,696</u>

10. Stock-Based Compensation

The Company maintains four equity compensation plans; the 2020 Stock Plan, or the 2020 Plan, the 2022 Stock Option and Incentive Plan, or the 2022 Plan, the 2022 Employee Stock Purchase Plan, or the ESPP, and the 2024 Inducement Plan, or the Inducement Plan. As of the Company's IPO in May 2022, the Company's board of directors determined that no further awards would be made under the 2020 Plan. The number of shares of common stock that may be issued under the 2022 Plan is subject to increase by the number of shares under any outstanding stock options forfeited and not exercised under the 2020 Plan. Additionally, the number of shares reserved for issuance under the 2022 Plan automatically increases on the first day of each fiscal year in an amount equal to the lower of (1) 5% of the shares of common stock outstanding on such date and (2) an amount determined by the Company's board of directors. The 2022 Plan allows the board of directors to grant incentive stock options, non-qualified stock options, stock appreciation rights, restricted stock awards, restricted stock units, unrestricted stock awards, cash-based awards, and dividend equivalent rights to the Company's officers, employees, directors and other key persons. The number of shares reserved for issuance under the ESPP automatically increases on the first day of each fiscal year in an amount equal to the lower of (1) 1% of the shares of common stock outstanding on such date and (2) an amount determined by the Company's board of directors.

As of December 31, 2024, 657,167 shares remained available for grant under the 2022 Plan and 397,998 shares remained available for issuance under the ESPP.

2024 Inducement Plan

In August 2024, the Company's board of directors adopted the Inducement Plan. The Inducement Plan provides for the grant of non-qualified stock options, stock appreciation rights, restricted stock awards, restricted stock units, unrestricted stock awards, dividend equivalent rights and other stock-based awards with respect to an aggregate of 1,000,000 shares of common stock (subject to adjustment as provided in the Inducement Plan). Awards under the Inducement Plan may only be granted to new employees who were not previously employed by the Company or its affiliates in accordance with the requirements of Nasdaq Stock Market Rule 5635(c)(4).

As of December 31, 2024, 702,184 shares remained available for issuance under the Inducement Plan.

Stock Option Valuation

In determining the fair value of the stock options granted, the Company uses Black-Scholes and the assumptions discussed below. Each of these inputs is subjective and generally requires significant judgment.

Expected Term—The Company's expected term represents the period that the Company's stock-based awards are expected to be outstanding. For stock options with service-based vesting periods, the expected term of the Company's stock options has been determined utilizing the "simplified" method for awards that qualify as "plain-vanilla" options.

Expected Volatility—The Company has historically been a private company and lacks significant company-specific historical and implied volatility information. The expected volatility is estimated based on a blend of the Company's own volatility and the average historical volatilities for comparable publicly traded biotechnology companies over a period equal to the expected term of the stock option grants. The comparable companies were chosen based on their similar size, stage in the

life cycle and area of specialty. The Company will continue to apply this process until enough historical information regarding the volatility of its own stock price becomes available.

Risk-Free Interest Rate—The risk-free interest rate is based on the U.S. Treasury zero coupon issues in effect at the time of grant for periods corresponding with the expected term of option.

Expected Dividend Yield—The Company has never paid dividends on its common stock and has no plans to pay dividends on its common stock. Therefore, the Company used an expected dividend yield of zero.

The fair value of stock options was estimated using the following weighted average assumptions:

	Year Ended December 31,	
	2024	2023
Risk-free interest rate %	4.15%	4.19%
Expected volatility %	81.33%	65.13%
Expected term (in years)	6.06	6.05
Expected dividend yield	—	—

Stock Option Activity

Stock option activity for the year ended December 31, 2024 was as follows:

	Stock Options	Weighted- Average Exercise Price	Weighted- Average Remaining Contractual Term (In Years)	Aggregate Intrinsic Value (In Thousands)
Outstanding as of December 31, 2023	4,233,203	\$ 10.83	8.4	\$ 2,147
Granted	2,175,133	14.13		
Exercised	(209,882)	10.62		
Canceled/Forfeited	(353,415)	13.23		
Outstanding as of December 31, 2024	5,845,039	\$ 11.92	8.0	\$ 578
Vested and exercisable as of December 31, 2024	2,467,174	\$ 9.92	7.0	\$ 565
Vested and expected to vest as of December 31, 2024	5,845,039	\$ 11.92	8.0	\$ 578

The aggregate intrinsic value of stock options is calculated as the difference between the exercise prices of the stock options and the fair value of the Company's common stock for those stock options that had exercises prices lower than the fair value of the Company's common stock. The total intrinsic value of the stock options exercised during the years ended December 31, 2024 and 2023 was \$1.0 million and \$1.4 million, respectively. The intrinsic value is the difference between the estimated fair value of the Company's common stock at the time of exercise and the exercise price of the stock option. During the years ended December 31, 2024 and 2023, the total proceeds to the Company from stock option exercises was \$2.2 million and \$0.2 million, respectively.

The weighted-average grant date fair value of stock options granted during the years ended December 31, 2024 and 2023 was \$10.19 and \$8.56 per share, respectively.

Restricted Stock Units

A restricted stock unit, or RSU, represents the right to receive one share of common stock upon vesting of the RSU. In February 2024, the Company granted employees a one-time RSU award that vests fully on the one-year anniversary of the grant date, provided that the employee remains employed with the Company. Certain employees, including employees who are executive officers of the Company, received a one-time RSU award that vests upon the achievement of certain performance-based clinical development milestones, or PSUs. Such awards cannot vest in less than one year, regardless of when the performance milestone is achieved. The Company's chief executive officer did not receive any RSU or PSU awards. A summary of the Company's RSU and PSU activity and related information for the year ended December 31, 2024 was as follows:

	Time-Based RSUs	PSUs	Weighted-Average Grant Date Fair Value
Outstanding as of December 31, 2023	—	—	\$ —
Granted	77,645	28,555	10.64
Vested	—	—	—
Forfeited	(4,920)	—	10.64
Issued and unvested as of December 31, 2024	72,725	28,555	\$ 10.64

The weighted average grant date fair value of the time-based RSUs and the PSUs granted during the year ended December 31, 2024 was \$10.64. As of December 31, 2024, there was \$0.1 million of unrecognized compensation costs related to unvested time-based RSUs, which are expected to be recognized over a weighted-average period of 0.1 years, and \$0.3 million of unrecognized compensation costs related to unvested PSUs, which are dependent upon achievement of the aforementioned clinical development milestones

Stock-Based Compensation Expense

Stock-based compensation expense recognized for stock option grants included in the accompanying consolidated statements of operations and comprehensive loss is as follows (in thousands):

	Year Ended December 31,	
	2024	2023
Research and development	\$ 5,012	\$ 2,966
General and administrative	6,445	4,082
Total stock-based compensation expense	<u>\$ 11,457</u>	<u>\$ 7,048</u>

The Company had 5,845,039 vested and unvested stock options outstanding as of December 31, 2024. As of December 31, 2024, total unrecognized compensation expense related to stock options was \$29.7 million. This amount is expected to be recognized over a weighted average period of approximately 2.6 years.

11. Income Taxes

The Company's loss before income taxes for the years ended December 31, 2024 and 2023 were generated in the following jurisdictions (in thousands):

	Year Ended December 31,	
	2024	2023
Domestic	\$ (87,466)	\$ (78,195)
Foreign	(3,132)	(358)
Worldwide	<u>\$ (90,598)</u>	<u>\$ (78,553)</u>

The components of net deferred income taxes consisted of the following as of December 31, 2024 and 2023 (in thousands):

	December 31,	
	2024	2023
Deferred tax assets:		
Net operating loss carryforwards	\$ 17,039	\$ 8,038
Research and development credits	7,769	4,547
Accrued expenses	864	577
Capitalized Section 174 R&D Costs	41,821	29,470
Stock compensation	4,511	2,510
Right-of-use liability	5,086	5,485
Intangible asset amortization	6,847	7,425
Other, net	4	21
Deferred tax assets	83,941	58,073
Deferred tax liabilities		
Right-of-use-Asset	(5,842)	(6,444)
Fixed Assets	(1,316)	(1,474)
Other, net	—	—
Deferred tax liabilities	(7,158)	(7,918)
Net deferred tax assets	76,783	50,155
Valuation allowance	(76,783)	(50,155)
Net deferred tax assets	<u>\$ —</u>	<u>\$ —</u>

The components of income tax expense were as follows for the years ended December 31, 2024 and 2023 (in thousands):

	Year Ended December 31,	
	2024	2023
Current expense:		
U.S. Federal	\$ —	\$ —
State	84	73
Foreign	(701)	—
Total current expense	(617)	73
Deferred expense:		
U.S. Federal	—	—
State	—	—
Foreign	—	—
Total deferred expense	—	—
Provision for income taxes	<u>\$ (617)</u>	<u>\$ 73</u>

A reconciliation of income tax expense to the amount computed by applying the statutory federal income tax rate to the loss from operations is summarized for the years ended December 31, 2024 and 2023, as follows:

	Year Ended December 31,	
	2024	2023
Tax at statutory rate	21.0%	21.0%
State tax (net of federal benefit)	(0.1)%	(0.7)%
Permanent differences	(0.8)%	(0.4)%
Research and development credit	3.4%	3.2%
GILTI Inclusion	0.0%	0.0%
U.K. R&D credit	0.0%	0.0%
Foreign rate differential	1.0%	0.0%
Change in valuation allowance	(23.6)%	(23.9)%
Other	(0.2)%	0.0%
Income tax expense (benefit)	0.7%	(0.8)%

On January 1, 2022, or the Transfer Date, the Company's wholly owned subsidiary, PepGen Limited, transferred all IP assets to the parent company, PepGen, in an arm's length transaction at fair value pursuant to an asset transfer agreement. The Company recognized a tax expense in 2022 of \$3.7 million, inclusive of a \$0.7 million unrecognized tax benefit. The Company's income tax benefit and expense was a net benefit of \$0.6 million for the year ended December 31, 2024 and expense of \$0.1 million for the year ended December 31, 2023. The income tax benefit for the year ended December 31, 2024 was due to the derecognition of an unrecognized tax benefit of \$0.7 million upon the dissolution of our U.K.-based entity, PepGen Limited on December 10, 2024. This is partially offset by \$0.1 million in state taxes on interest income generated from the Company's cash equivalents and marketable securities. The income tax expense for the year ended December 31, 2023 consisted of state taxes on interest income generated from the Company's cash equivalents and marketable securities.

The Company has federal net operating losses, or NOLs, of \$58.2 million and federal research and development, or R&D, credits of approximately \$9.1 million as of December 31, 2024, before consideration of limitations under IRC Section 382 of the Internal Revenue Code of 1986, as amended, or Section 383, as further described below. The federal NOLs do not expire, but generally limit the NOLs deduction to the lesser of the NOL carryover or 80% of a corporation's taxable income. The tax credits will begin to expire in 2042. As of December 31, 2024, the Company has state NOLs of \$76.6 million and state research and development credits of \$1.8 million. The state NOLs will begin to expire in 2041, and the tax credits will begin to expire in 2037.

Net operating loss and tax credit carryforwards may become subject to an annual limitation in the event of certain cumulative changes in the ownership interest of significant stockholders over a three-year period in excess of 50%, as defined under Sections 382 and 383 of the IRC, respectively, as well as similar state provisions. This could limit the amount of tax attributes that can be utilized annually to offset future taxable income or tax liabilities. The amount of the annual limitation is determined based on the value of the Company immediately prior to the ownership change. Subsequent ownership changes may further affect the limitation in future years. An assessment of such ownership changes under Section 382 was not completed through December 31, 2024. To the extent that an assessment is completed in the future, the Company's ability to utilize tax attributes could be restricted on a year-by-year basis and certain attributes could expire before they are utilized. The Company will examine the impact of any potential ownership changes in the future. A full valuation allowance has been provided against the deferred tax assets related to the Company's net operating loss and tax credits carryforwards and, if an adjustment is required, this adjustment would be offset by an adjustment to the valuation allowance.

The Company files tax returns as prescribed by the tax laws of the jurisdictions in which it operates. In a normal course of business, the Company is subject to examination by U.S. federal and state as well as foreign jurisdictions, where applicable. The Company's tax years are still open since inception. To the extent that the Company has tax attribute carryforwards, the tax year in which the attributes were generated may still be adjusted upon examination by the U.S. Internal Revenue Services or state tax authorities to the extent utilized in a future period. The Company is not currently under examination by any tax authorities.

The following table summarizes the reconciliation of the beginning and ending amount of total unrecognized tax benefits recorded in the statement of operations for each of the periods indicated:

	December 31,	
	2024	2023
Balance at beginning of the period	\$ 713	\$ 673
Increase related to current year tax positions	—	—
Increase related to prior year tax positions	—	—
Decrease related to prior year tax positions	(701)	—
Currency translation	(12)	40
Balance at the end of the period	<u>\$ —</u>	<u>\$ 713</u>

The Company's policy is to recognize interest and/or penalties related to income tax matters in income tax expense. The Company released approximately \$0.7 million in unrecognized tax benefits due to the liquidation of its UK subsidiary, PepGen Limited. As of December 31, 2024, the Company had no unrecognized tax benefits or accrued interest or penalties.

12. Segment Reporting

ASU 2023-07 establishes standards for reporting information about operating segments on a basis consistent with the Company's internal organization structure as well as information about services categories, business segments and major customers in financial statements.

Segment reporting is prepared on the same basis that the chief executive officer, who is the Company's chief operating decision maker and manages the business, makes business decisions and assesses performance. The Company has one reportable segment and regularly reviews operating expenses and net loss on a consolidated basis. The Company operates in one location in Boston, Massachusetts focused on advancing oligonucleotide therapeutics with the goal of transforming the treatment of severe neuromuscular and neurologic diseases. The Company tracks external operating expenses on a program-by-program basis. Net loss is comprised of expenses related to our two lead product candidates and other personnel, facility, and general and administrative costs. Operating expenses and net loss are the basis the chief operating decision maker uses for the purpose of deciding how to allocate resources, specifically on a program basis as presented below.

The chief operating decision maker uses operating expenses and net loss to evaluate progress on research and development activities on the Company's two lead product candidates as well as when making strategic decisions regarding the Company's pipeline. Operating expenses and loss are also used to monitor budget versus actual results.

The following table outlines the Company's functional operating expenses:

	Year Ended	
	2024	2023
Research and Development Expenses		
PGN-EDO51 direct research and development expenses	\$ 19,195	\$ 21,369
PGN-EDODM1 direct research and development expenses	21,265	16,486
Platform and external research and development expenses	2,556	4,762
Personnel-related (including stock-based compensation)	23,433	16,143
Facility related and other	5,819	5,165
Other research and development expenses	4,210	4,201
Total research and development expense	76,478	68,126
General and Administrative Expenses		
Personnel-related (including stock-based compensation)	12,449	8,198
Facility related and other	1,987	1,504
Other general and administrative	6,825	6,938
Total general and administrative expense	21,261	16,640
Loss from operations	(97,739)	(84,766)
Other income (expense):		
Interest income	7,142	6,400
Other (expense) income, net	(1)	(187)
Total other income (expense), net	7,141	6,213
Income tax expense	617	(73)
Net loss	<u>\$ (89,981)</u>	<u>\$ (78,626)</u>



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