



PepGen Inc.

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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, 2022

OR

TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934 FOR THE
TRANSITION PERIOD FROM _____ TO _____

Commission File Number 001-41374

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

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

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

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 March 15, 2023, was \$114.2 million. The number of shares of Registrant's Common Stock outstanding as of March 15, 2023 was 23,781,905.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's Definitive Proxy Statement relating to its 2023 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 and foreign countries;
- our ability to contract with third-party suppliers and manufacturers and their ability to perform adequately;
- 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 effect of the ongoing COVID-19 pandemic, 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 Securities and Exchange Commission 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 Annual Report on Form 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 very early in our development efforts. We have only advanced one product candidate into clinical development, 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 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 those of the Phase 1 study of PGN-EDO51, are not necessarily predictive of the results of later preclinical studies and any clinical trials of our product candidates. We have only entered clinical trials for one of our product candidates and 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 planned clinical trials or failure to demonstrate safety and efficacy to the satisfaction of applicable regulatory authorities could prevent us from commercializing any 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 and preclinical and clinical testing, and these third parties may not perform satisfactorily or, dedicate adequate resources to meet our needs, or may be unable to acquire the necessary supplies to perform successfully.
- 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 EDO 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 development and regulatory 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 may be volatile and fluctuate 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 Annual Report on Form 10-K, as well as in other documents that we file with the U.S. Securities and Exchange Commission (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

We are 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 Enhanced Delivery Oligonucleotide, or EDO, platform is founded on over a decade of research and development and leverages cell-penetrating peptides to improve the uptake and activity of conjugated oligonucleotide therapeutics. This technology was initially developed through a collaboration between researchers at the University of Oxford and the Medical Research Council of United Kingdom Research and Innovation. We have licensed an extensive patent portfolio from these institutions to support the further advancement and potential commercialization of our EDO platform. 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 and the central nervous system, or CNS. Furthermore, the high levels of pharmacological activity observed in preclinical studies support our belief that our EDO platform technology has the potential to deliver therapeutic agents to the cell nucleus. Using these EDO peptides, we are generating a pipeline of oligonucleotide therapeutic candidates that target the root cause of serious diseases.

We are currently in clinical-stage development and completed a first-in-human Phase 1 clinical trial in healthy volunteers, or HV, with our lead product candidate, PGN-EDO51, in the third quarter of 2022. We are developing PGN-EDO51 to treat individuals with Duchenne muscular dystrophy, or DMD, whose mutations are amenable to an exon 51-skipping therapeutic approach. An exon is a segment of a gene that – together with other exons – contains the code that is translated into a protein. Exon skipping is a therapeutic modality that enables mutations in the gene to be bypassed, thereby repairing this code and enabling production of a truncated, yet functional version of the target protein. In a Phase 1 clinical trial, treatment with PGN-EDO51 resulted in the highest levels of exon skipping and oligonucleotide delivery in humans following a single dose when compared to publicly available data for other approaches. PGN-EDO51 was found to be generally well-tolerated at pharmacologically relevant dose levels in this study. In non-human primate, or NHP, studies, PGN-EDO51 at a dose of 30 mg/kg achieved over 70% exon 51 skipping in skeletal muscle, including diaphragm, and in *mdx* mouse studies, dystrophin levels of over 80% were observed in skeletal muscle following a single 60 mg/kg dose of PGN-EDO23, the murine analogue of PGN-EDO51. These results represent what we believe to be the highest level of exon 51 skipping in NHP skeletal muscle at tolerable target dose levels, and the highest level of dystrophin production in *mdx* mouse skeletal muscle when compared to other clinical-stage DMD therapeutic candidates. In addition, in head-to-head NHP studies, we observed that PGN-EDO51 had greater activity than R₆G-PMO, which we believe to be structurally equivalent to Sarepta Therapeutics, Inc.'s, or Sarepta's, SRP-5051, the most clinically advanced peptide-ASO conjugate. Moving forward, our clinical development program comprises two, parallel Phase 2 studies of PGN-EDO51 in DMD patients whose disease is amenable to an exon 51 skipping approach. The first study, CONNECT1-EDO51, is expected to be an open-label, multiple ascending dose, or MAD, study to open in Canada in the first half of 2023, with initial dystrophin, exon skipping and safety data anticipated in 2024. The second study, CONNECT2-EDO51, is expected to be a global, randomized, double-blind, placebo-controlled MAD clinical trial, or RCT, anticipated to open in the second half of 2023, pending clearance by the U.S. Food and Drug Administration, or FDA, of an Investigational New Drug, or IND filing, and/or clearance by the European Medicines Agency of a Clinical Trial Application, or CTA, in each case, anticipated in the second half of this year. Learnings from the open-label Phase 2 study will inform the conduct of the global RCT which is intended to support a potential accelerated approval pathway for PGN-EDO51. Building on the high levels of exon skipping and tissue concentration observed in our Phase 1 trial, we believe that repeat dosing of PGN-EDO51 may lead to the accumulation of exon 51 skipped transcript and dystrophin protein in patients, which may in turn drive meaningful clinical benefit for those who live with this devastating, progressive, life-shortening disease.

We are also developing PGN-EDODM1 for the treatment of myotonic dystrophy type 1, or DM1, and are utilizing what we believe to be a unique mechanism of action. The therapeutic oligonucleotide component of PGN-EDODM1 is engineered to bind to the cytosine-uracil-guanine (CUG) repeat expansion present in the *DMPK* mRNA of DM1 patients, thus potentially reducing the ability of these trinucleotide repeats to sequester MBNL1, a critical transcription factor. The liberation of MBNL1 in turn leads to the correction of downstream mis-splicing events that are evident in DM1, and thus we believe this approach – which is not designed to knock down *DPMK* – is intended to directly address the underlying genetic defect of this disease. Treatment with PGN-EDODM1 resulted in the robust correction of mis-splicing in preclinical models with both long and short CTG repeats, including in the HSALR mouse model, where complete reversal of myotonia was also observed following a single dose. Furthermore, the oligonucleotide concentrations that were observed to be pharmacologically active in this mouse model of DM1 were found to be comparable to the tissue concentrations of oligonucleotide in human muscle observed in our clinical trial of PGN-EDO51. We expect to open our FREEDOM-DM1 Phase 1 randomized, placebo-controlled single ascending dose, or SAD, clinical trial of PGN-EDODM1, in DM1 patients in the first half of 2023, with functional assessments, correction of mis-splicing and safety data anticipated in 2024. Based on data obtained in our Phase 1 HV study of PGN-EDO51, we believe that PGN-EDODM1 has the potential to achieve tissue concentrations in people living with DM1 that could lead to clinically meaningful outcomes.

In addition to these lead candidates, we are developing EDO therapeutics for further DMD exon skipping populations, including exon 53-, 45- and exon 44-skipping amenable patients, and have observed robust exon skipping levels in NHP for our PGN-EDO53 program, and in wild-type human cells for our PGN-EDO45 and PGN-EDO44 programs. We have also initiated research efforts for additional indications, including neuromuscular diseases and neurologic disorders, and from this pipeline of candidates we anticipate advancing additional programs into clinical trial application, or CTA and investigational new drug, or IND-enabling studies in 2024.

The advent of oligonucleotide therapeutics represented a major advance in the history of the biopharmaceutical industry. Oligonucleotide therapeutics are a nucleic acid-based genetic medicine modality that is designed to target the root cause of many diseases through the modulation of RNA expression and processing. These therapeutics have demonstrated clinical benefit and been approved for the treatment of multiple diseases. The approved drugs within this category include antisense oligonucleotides, or ASOs, which are short, synthetic, single-stranded oligonucleotides designed to inhibit or modify expression of protein and RNA.

However, despite the considerable potential of oligonucleotides as a therapeutic class, the challenges associated with their delivery has limited the development of these therapies in certain disease areas. On their own, oligonucleotide therapeutics are not readily distributed to heart and skeletal muscle, the key tissues affected in neuromuscular diseases, and are not efficiently taken up into these cells.

Our EDO Platform

To address this challenge, we engineered our proprietary EDO technology to optimize tissue penetration, cellular uptake and nuclear delivery, which we believe may enhance the therapeutic activity of oligonucleotides and improve the tolerability of these genetic medicines. Our platform is based on novel cell-penetrating EDO peptides that were developed through an iterative process which selected simultaneously for high cellular uptake, biodistribution to key muscle targets, including cardiac tissue, and improved tolerability. We utilize phosphorodiamidate morpholino oligomers, or PMOs, a type of ASO chemistry that confers enhanced stability, 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. We are continuing to build and develop this platform technology as we expand into new therapeutic areas.

Using this novel, proprietary platform, we are developing a broad pipeline of disease-modifying EDO candidates to treat a variety of degenerative neuromuscular and neurologic diseases. Our platform is designed to offer the following advantages compared to existing oligonucleotide approaches:

- Enhanced delivery to skeletal muscle, including diaphragm, cardiac muscle and the CNS.
- Improved activity, which we have observed in a clinical trial and in preclinical studies:
 - In healthy volunteers, we observed the highest levels of exon skipping and oligonucleotide delivery in humans following a single dose of PGN-EDO51 when compared to publicly available data for other exon 51 skipping approaches;
 - In NHPs, we observed what we believe to be the highest rate of exon 51 skipping in skeletal muscles, including the diaphragm, at tolerable target dose levels of PGN-EDO51 compared to the reported data for any approved therapeutic or known developmental candidate;
 - In the *mdx* mouse model, we observed the highest level of dystrophin production in skeletal muscle following a single dose of PGN-EDO23, the murine analogue of PGN-EDO51, when compared to what has been reported for clinical-stage DMD therapeutic candidates.
- An enhanced balance between activity and tolerability, which is designed to afford our product candidates a wider therapeutic index.
- Robust, scalable and cost-efficient manufacturing that does not require cell-based processes.
- Accelerated and efficient pipeline development of therapeutic candidates enabled by use of the same EDO peptide across all our initial programs.

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 and to exhibit a favorable tolerability profile. 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 five programs. We anticipate expanding this pipeline to include other neuromuscular targets as well as opportunities in neurologic indications and intend to leverage the modular, scalable nature of our EDO technology to support our expansion into these new therapeutic areas. Our lead product candidates, PGN-EDO51 and PGN-EDODM1, target a large potential market opportunity, with approximately 135,000 DMD exon 51

and DM1 patients across the United States, Europe and Japan, and we own worldwide development and commercialization rights to all our programs.

PROGRAM	INDICATION TARGET	DISCOVERY	PRECLINICAL	PHASE 1	PHASE 2	REGISTRATIONAL*
PGN-EDO51	Duchenne muscular dystrophy Exon 51					
PGN-EDODM1	Myotonic dystrophy type 1 DMPK					
PGN-EDO53	Duchenne muscular dystrophy Exon 53					
PGN-EDO45	Duchenne muscular dystrophy Exon 45					
PGN-EDO44	Duchenne muscular dystrophy Exon 44					
FUTURE PIPELINE OPPORTUNITIES						
Additional neuromuscular indications						
Neurologic indications						

PGN-EDO51

Our lead product candidate is PGN-EDO51, an EDO peptide conjugated to a PMO therapeutic cargo, which we are developing for the treatment of DMD patients with mutations amenable to an exon 51-skipping approach. DMD is a debilitating X-linked recessive muscle-wasting disease that predominantly affects boys, and arises due to the presence of mutations in the gene encoding dystrophin, a protein necessary for normal muscle function. It is one of the most prevalent rare genetic diseases globally, with up to 15,000 DMD patients in the United States, approximately 25,000 DMD patients in Europe and 5,000 in Japan. It is thought that 13% of patients with DMD have mutations that are amenable to treatment with an exon 51-skipping therapeutic approach, and thus the estimated exon 51 patient population is approximately 2,000 in the United States, 3,200 in Europe and 700 in Japan. DMD patients typically succumb to cardiac and respiratory failure in their early adulthood with a mean lifespan of approximately 25 years. There is no cure for DMD and there are no treatments that have clinically demonstrated a meaningful impact on disease progression.

PGN-EDO51 is designed to splice out exon 51 of the dystrophin pre-mRNA, resulting in the restoration of the open reading frame of the dystrophin transcript and the production of a shortened, yet functional dystrophin protein. In a Phase 1 clinical trial of PGN-EDO51, we observed the highest levels of exon skipping and oligonucleotide concentration in muscle in humans following a single dose, when compared to publicly available data for other exon 51 skipping approaches. In wild-type NHP studies, at tolerable doses, we have observed what we believe is the highest rate of exon 51 skipping in skeletal muscle, including diaphragm, based on cross-trial comparisons with publicly available data for any approved therapeutic or known developmental candidate. These cross-trial comparisons were conducted with data published by Sarepta for EXONDYS 51® (eteplirsen), and by Dyne Therapeutics, Inc, or Dyne for DYNE-251. In addition, in head-to-head NHP studies, we observed that PGN-EDO51 had greater activity than R₆G-PMO at the same dose level, a comparator compound that we believe to be structurally equivalent to Sarepta's SRP-5051, the most clinically advanced peptide-ASO conjugate. At a dose of 10 mg/kg, PGN-EDO51 exhibited approximately as much exon skipping activity as a 3-fold higher dose, i.e., 30 mg/kg, of R₆G-PMO. In the *mdx* mouse model, we observed the highest level of dystrophin production in skeletal muscle following a single dose of PGN-EDO23, the murine analogue of PGN-EDO51, when compared to other clinical-stage DMD therapeutic candidates. Our Phase 1 clinical trial also indicated that PGN-EDO51 was generally well-tolerated at pharmacologically relevant dose levels. In 2023, we anticipate opening two clinical trials in DMD patients amenable to an exon 51 skipping approach. CONNECT1-EDO51 is an open-label MAD study to open in Canada in the first half of 2023, with initial dystrophin, exon skipping and safety data anticipated in 2024. CONNECT2-EDO51 is a multinational, randomized, placebo-controlled MAD clinical trial anticipated to open in the second half of 2023, and is designed to potentially support a future potential accelerated approval pathway.

PGN-EDODM1

We are developing PGN-EDODM1, an EDO peptide-conjugated PMO, for the treatment of DM1. DM1 is a monogenic, autosomal dominant, progressive disorder that primarily affects skeletal, cardiac and smooth muscles as well as the CNS, resulting in significant physical, cognitive and behavioral impairments and disability. The burden of disease is significant, and many patients have

a shortened lifespan. DM1 is caused by an abnormal trinucleotide repeat expansion in a region of the *DMPK* gene and is estimated to affect approximately 40,000 patients in the United States, 75,000 patients in Europe and 15,000 patients in Japan. There are currently no approved therapies for the treatment of DM1.

PGN-EDODM1 leverages the same EDO peptide as PGN-EDO51 to deliver a PMO into muscle cells that binds to the cytosine-uracil-guanine, or CUG, trinucleotide repeat expansion present in the *DMPK* mRNA, thus reducing the ability of these trinucleotide repeats to sequester 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 *ex vivo*, we observed that treatment with PGN-EDODM1 led to the robust correction of multiple downstream mis-spliced transcripts and a reduction in toxic nuclear foci. In our *in vivo* preclinical studies, a single dose of PGN-EDODM1 was observed to correct the molecular and functional phenotypes presented in the human skeletal actin – long repeat, or HSA^{LR}, mouse model of disease, ameliorating downstream mis-splicing events, reversing myotonia and normalizing mobility. We also observed that the molecular correction effected by PGN-EDODM1 in this preclinical mouse model exhibited a durability of effect that was in excess of six months. Furthermore, the tissue concentrations of oligonucleotide that were found to be pharmacologically active in the HSA^{LR} mouse model were similar to those observed for PGN-EDO51 in human muscle in a Phase 1 study, supporting our belief in the ability of PGN-EDODM1 to achieve potentially safe and effective therapeutic levels of oligonucleotide in the clinic. We expect to open our FREEDOM-DM1 Phase 1, randomized, placebo-controlled SAD clinical trial of PGN-EDODM1 in DM1 patients in the first half of 2023, with functional assessments, correction of mis-splicing and safety data anticipated in 2024.

Additional DMD Programs

We are developing additional EDO therapeutics for further DMD patient populations, including PGN-EDO53, for the 8% of DMD patients who are amenable to an exon 53-skipping approach, PGN-EDO45, for the 8% of DMD patients who are amenable to an exon 45-skipping approach, and PGN-EDO44, for the 6% of DMD patients who are amenable to an exon 44-skipping approach. These programs utilize the same EDO cell penetrating peptide as our exon 51-skipping product candidate, PGN-EDO51, which we believe will allow us to leverage our drug development experience with this peptide, and in this indication, to rapidly drive our exon 53, 45 and 44-skipping product candidates forward. In a NHP study of PGN-EDO53, we observed single-dose exon skipping levels that were almost seven times higher than those observed for R₆G-PMO53, a relevant comparator peptide-PMO conjugate approach. For PGN-EDO45, high, dose-dependent levels of exon skipping were observed in wild-type human myoblasts, with our nominated candidate outperforming the R₆G-PMO45 comparator at every dose level assessed. Finally, our PGN-EDO44 nominated candidate also exhibited high, dose-dependent levels of exon skipping in wild-type human myoblasts. We anticipate providing further updates on these programs as preclinical development continues.

Expanding the Applications and Scope of Our EDO Platform

New indications with PMO therapeutics

We intend to leverage our deep understanding of our EDO platform and oligonucleotide therapeutic candidates to develop additional product candidates for other indications. We believe the ability of our EDO technology to deliver exon skipping therapeutics to muscle cells, including cardiac muscle cells, as well as the CNS is largely independent of the exact sequence of the PMO. As such, by leveraging our preclinical data and the plug-and-play nature of our EDO platform, we believe that we are well positioned to develop additional product candidates with the potential to drive clinically relevant therapeutic outcomes in other neuromuscular diseases as well as neurologic indications.

New cargos

We believe that our EDO technology has the potential to facilitate the delivery of multiple classes of oligonucleotide therapeutics. To date, our efforts have primarily focused on the delivery of PMOs, but we are also actively pursuing 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 cell penetrating peptides. We will leverage our extensive experience in this field to design new peptides that target specific tissue types, and will seek to further optimize the tissue, cellular and nuclear delivery of our EDO platform technology.

Our Culture and Team

Our mission is to deliver transformative therapeutics to those in need, and we believe our innovative 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 and corporate development. 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; Jaya Goyal, Ph.D., our Executive Vice President of Research and Preclinical Development, who has held roles at Wave Life Sciences Ltd., and Biogen Inc., and brings considerable experience in bioanalytical studies, biomarkers and pharmacology across a broad range of preclinical-, clinical- and commercial-stage programs; Michelle L. Mellion, M.D., our Senior Vice President, Clinical Development, who is double Board-certified in neurology and clinical neurophysiology and has held roles at Fulcrum Therapeutics, Inc., Vertex Pharmaceuticals, Inc., and Biogen Inc; Niels Svenstrup, Ph.D., our Senior Vice President of Chemistry, Manufacturing and Control, who has extensive experience in the manufacturing and release of peptide drugs for late-stage clinical programs and has held roles at Ascendis Pharma A/S, Cydan LLC, and Lundbeck A/S, amongst others. We have established a strong scientific advisory board, 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 the Medical Research Council of United Kingdom Research and Innovation 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.

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 our lead product candidate, PGN-EDO51, through clinical trials and potential regulatory approval.** We are developing PGN-EDO51 to treat individuals with DMD whose mutations are amenable to an exon 51-skipping therapeutic approach. There is no cure for DMD and there are no treatments that have demonstrated a significant impact on disease progression in the clinic. In a Phase 1 clinical trial of PGN-EDO51, we observed the highest levels of exon skipping and oligonucleotide delivery to muscle in humans following a single dose when compared to publicly available data for other exon 51 skipping approaches. In wild-type NHP studies, we observed what we believe to be the highest rate of exon 51 skipping in skeletal muscle, including the diaphragm, at tolerable target dose levels when compared to any approved therapeutic or known developmental candidate, and in *mdx* mice we observed the highest level of dystrophin production in skeletal muscle following a single dose when compared to such data reported for other clinical-stage DMD candidates. Furthermore, in a head-to-head study conducted in NHP, we observed that PGN-EDO51 had greater activity than R6G-PMO at the same clinically-relevant dose level, a comparator compound that we believe to be structurally equivalent to Sarepta's SRP-5051, the most clinically advanced peptide-ASO conjugate. In our Phase 1 clinical trial, we also observed that PGN-EDO51 was generally well-tolerated at pharmacologically relevant dose levels. In 2023, we anticipate opening two clinical trials in DMD patients amenable to an exon 51 skipping. CONNECT1-EDO51 is an open-label MAD study to open in Canada in the first half of 2023, with initial dystrophin, exon skipping and safety data anticipated in 2024. CONNECT2-EDO51 is a multinational, randomized, placebo-controlled MAD clinical trial anticipated to open in the second half of 2023, and is designed to potentially support a future accelerated approval pathway.
- **Advance PGN-EDODM1 through clinical trials and potential regulatory approval.** We are developing PGN-EDODM1 for the treatment of patients with DM1, and have observed robust pharmacological activity in preclinical models with both long and short CTG repeats. In a mouse model of DM1 we have observed that a single dose of PGN-EDODM1 corrected mis-splicing resulting in resolution of myotonia and improved mobility that was maintained for at least six months. The tissue concentrations of oligonucleotide that were found to be pharmacologically active in the HSA^{LR} mouse model were similar to those observed for PGN-EDO51 in human muscle in a Phase 1 study, supporting the ability of PGN-EDODM1 to achieve potentially therapeutic levels of oligonucleotide in the clinic. We believe that PGN-EDODM1 has the potential to

transform the treatment of DM1, and we expect to open our FREEDOM-DM1 Phase 1, randomized, placebo-controlled SAD clinical trial of PGN-EDODM1 in DM1 patients in the first half of 2023. Functional assessments, correction of mis-splicing and safety data from this trial are anticipated in 2024. Furthermore, we believe that the successful development of PGN-EDODM1 would further support the EDO platform and demonstrate its potential to generate therapeutic candidates in neuromuscular indications beyond DMD.

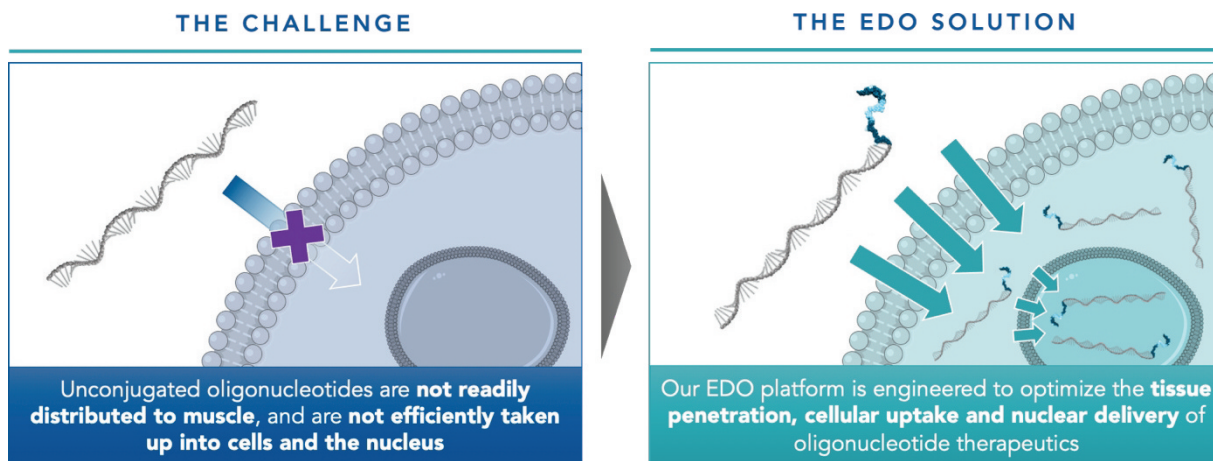
- **Expand our pipeline of oligonucleotide therapeutic candidates for the treatment of additional DMD patient populations.** We aim to expand our portfolio by pursuing additional programs where our EDO technology could improve clinical activity relative to current therapeutic approaches and address areas of great unmet need. For example, approximately one third of the mutations that cause DMD could be treated by exon-skipping therapeutics directed against exons 51, 53, 45 and 44. We are employing the same EDO technology used in PGN-EDO51 and PGN-EDODM1 for PGN-EDO53, PGN-EDO45 and PGN-EDO44, our exon-skipping therapeutic candidates for the treatment of individuals with DMD whose mutations are amenable to treatment with exon 53-, 45- and 44-skipping approaches respectively. We have observed high levels of exon skipping in NHP for PGN-EDO53, and in wild-type human cells for PGN-EDO45 and PGN-EDO44, and anticipate providing further updates on these programs as development progresses.
- **Leverage the full potential of our EDO technology to expand into other neuromuscular, neurological and cardiac disease areas.** We have observed both clinically and preclinically that our EDO technology has the potential to efficiently deliver nucleic acid payloads such as ASOs to muscle cells, including cardiac muscle cells, and into key regions of the brain in NHP. We are looking to develop disease-modifying peptide-conjugated oligonucleotide candidates for the potential treatment of a variety of other neuromuscular and neurological indications and will assess alternative routes of administration, including intrathecal, as part of this process.
- **Utilize the modular nature of our EDO platform to evaluate new cargos and peptide technologies.** We continue to optimize our EDO technology to increase our ability to drive the biodistribution of our conjugates to desired target tissues in the body. To accomplish this, we have built and continue to build our peptide chemistry and biology groups to further explore the structure-activity relationship of our existing EDO platform and to develop new delivery peptides. These next-generation peptides may allow us to develop potential disease-modifying therapeutic candidates for an expanded range of target indications. Furthermore, 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 we will thus seek 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; to the advancement of our programs in maximizing their market potential; or to the expansion of our platform capabilities.

Our EDO Platform

Overview

Our proprietary EDO platform is based on a novel, unique class of cell-penetrating peptides, or CPPs, that were designed to meaningfully enhance the tissue penetration, cellular uptake and nuclear delivery of oligonucleotide therapeutics. This technology is founded on over a decade of research and development that focused on improving the therapeutic utility of CPPs, resulting in a library of EDO peptides that mitigate the tolerability challenges observed with earlier cell-penetrating peptides. Using these EDO peptides, we are generating a pipeline of peptide-conjugated oligonucleotide therapeutic candidates that are engineered to successfully target the root cause of serious diseases and to exhibit a favorable tolerability profile. We believe that our approach to oligonucleotide delivery is potentially best-in-class, a belief that is supported by our observation of the highest levels of exon skipping and oligonucleotide delivery in humans following a single dose of PGN-EDO51 when compared to publicly available data for other exon 51 skipping approaches, and a generally well-tolerated profile for this product candidate observed, to date, at pharmacologically relevant dose levels. In wild-type NHP studies, we observed what we believe to be the highest rate of exon 51 skipping in skeletal muscle, including the diaphragm, at tolerable target dose levels compared to any approved therapeutic or known developmental candidate, and in *mdx* mice we observed the highest level of dystrophin production in skeletal muscle following a single dose when compared to other clinical-stage DMD candidates. For these human, NHP, and murine studies, such comparisons were conducted both across different trials with publicly available information, and in some instances with data obtained from head-to-head studies, and encompass unconjugated, peptide-conjugated, antigen binding fragment-conjugated and monoclonal antibody-conjugated oligonucleotide therapeutic approaches. The totality of the clinical and preclinical datasets that underpin our EDO technology highlight the potential ability of our CPP platform to address critical disease phenotypes in neuromuscular indications like DMD and DM1, with our lead

EDO therapeutic candidates being focused on these two indications. Our peptides also enable delivery of oligonucleotides across the blood-brain barrier, a characteristic which could support the future development of EDO therapeutics for neurologic indications.



Our EDO technology is designed to address the delivery challenges that limit oligonucleotide therapeutics.

The Therapeutic Potential of Oligonucleotides

The central dogma of biology—the transcription of DNA into RNA, and the subsequent translation of RNA into proteins—describes the flow of genetic information within the cell. DNA plays a critical, fundamental role in all biological processes, and while there exists considerable variation in the genetic code across the human population, certain alterations, or mutations, in an individual's DNA sequence can lead to deleterious outcomes and disease pathologies. A genetic disease can be caused by a mutation in a single gene, known as a monogenic disorder, or by mutations in multiple genes, known as a multifactorial inheritance disorder. The term 'genetic medicine' encompasses disease-modifying therapeutic agents that are designed to alter and correct genetic mutations at the DNA or RNA level. These therapeutic agents can be divided into four categories – viral vector gene therapies, DNA/RNA editing approaches, small molecules and oligonucleotide therapeutics. Significant progress has been made in the field of genetic medicine over the last decade, and a number of genetic medicines have been approved or are in clinical development.

Oligonucleotide therapeutics are a nucleic acid-based genetic medicine modality that are designed to target the root cause of many diseases 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 genes, and each of these approaches can lead to profound biological effects.

The advent of oligonucleotide therapeutics represented a major advance in the history of the biopharmaceutical industry. Oligonucleotide therapeutics consist of strings of nucleotides, the building blocks of RNA and DNA, and mimic the structures of active nucleic acids in the body to reproduce or expand upon the typical activities of these species. The development of oligonucleotide therapeutics has increased the arsenal of potential therapeutic modalities and has enabled the targeting of a diverse set of diseases that have proven difficult to treat through other approaches. These therapeutic candidates are built around the sequences of their target RNA/DNA molecules, which offers them a high degree of specificity and affords them the ability to target pathogenic mutations and processes that cannot easily be addressed by conventional drugs. Oligonucleotide therapeutics have demonstrated clinical benefit and been approved for the treatment of multiple diseases, such as spinal muscular atrophy, 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 via complementary Watson-Crick base pairing, 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 a particular mRNA through the RNA interference, or RNAi, pathway. Across approved oligonucleotide therapeutics, in 2020, approximately \$3.2 billion in sales were generated.

Therapeutic oligonucleotides 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. The resulting oligonucleotides – 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 reached the clinic in a number of indications, including DMD. Sarepta’s marketed drug EXONDYS 51[®] (eteplirsen) is a PMO that was approved in 2016 but has left much room for improvement given its relatively low tissue and cell penetration and minimal induction of dystrophin production. Despite these challenges, EXONDYS 51[®] generated approximately \$454 million in sales in the United States and Israel in 2021.

The Challenge of Oligonucleotide Delivery

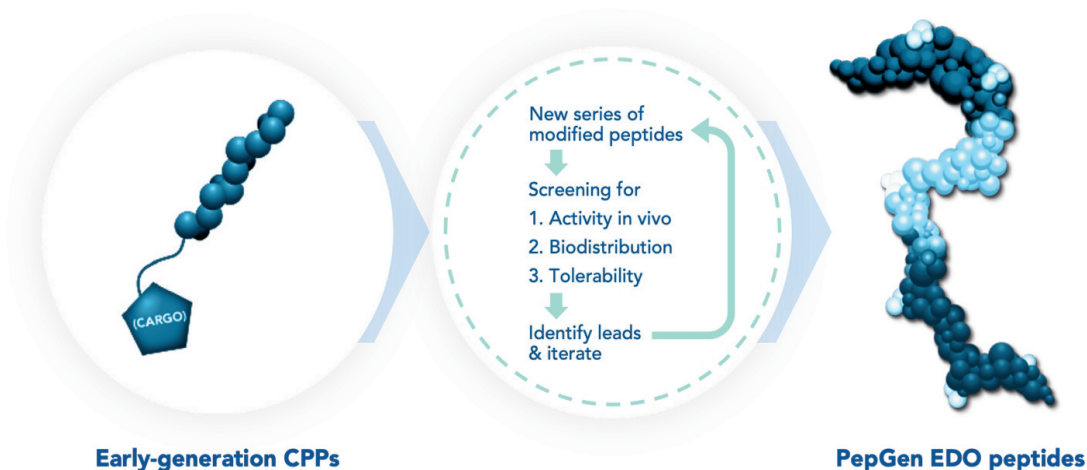
In order for oligonucleotide therapeutics to exert their intended effect, they must first gain access to the intracellular space where RNA processing and translation occurs. Historically, the delivery of oligonucleotides to the interior of the cell proved challenging due to their high molecular weight and the lack of a specific mechanism to facilitate their transport across the cell membrane and into 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 cell-penetrating peptides, or CPPs. CPPs are designed to facilitate the transport of oligonucleotides across the plasma membrane, thus allowing these cargo species to reach their intracellular site of action. 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

We engineered our proprietary EDO technology to optimize tissue penetration, cellular uptake and nuclear delivery, which we believe may enhance the therapeutic activity and improve the tolerability of oligonucleotide therapeutics. Our platform is based on novel cell-penetrating peptide technology, and our delivery vectors possess four key structural characteristics:

- Two positively charged, arginine-rich regions, one at the N-terminus and the other at the C-terminus;
- The interspersions of a specifically selected non-natural amino acid within the arginine-rich regions – these residues provide stability in the physiological environment, and confer other beneficial properties;
- A central core rich in hydrophobic residues that separates the arginine-rich regions and plays a critical role in tissue and cell uptake;
- A proprietary linker that plays a key role in modulating the therapeutic index of the resulting EDO conjugate.

Our EDO peptides were developed through an iterative optimization process that selected simultaneously for biodistribution to key muscle targets, including cardiac tissue; high cellular uptake; endosomal escape, where the therapeutic agent is released from the endosome sub-cellular compartment in a functional form; delivery to the cell nucleus; and reduced toxicity. 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. We are continuing to build and develop this platform technology as we expand into new therapeutic areas.



We optimized EDO peptides for properties that we believe are essential for therapeutics.

Advantages of Our Approach

Using our novel EDO platform, we are developing a broad pipeline of disease-modifying peptide-conjugated oligonucleotide candidates to treat a variety of degenerative neuromuscular diseases. 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 skeletal muscle, including diaphragm, cardiac muscle and the CNS:** We have observed in preclinical studies that our peptides delivered their cargo oligonucleotide therapeutics to key neuromuscular tissues, allowing us to address multiple disease pathologies in multi-systemic indications such as DMD and DM1. Furthermore, we believe our EDO peptides support the ability to promote endosomal escape and facilitate the robust delivery of cargo oligonucleotides to the cell nucleus. This differentiating feature of our EDO platform has been observed in mice and NHPs across multiple tissue types, including those critical to neuromuscular indications – skeletal, smooth and cardiac muscle. We believe the ability of our EDO peptide to deliver oligonucleotides to the CNS could potentially address neurological phenotypes in these diseases as well.
- **Improved activity, which we have observed in a Phase 1 clinical study, in NHPs and in *mdx* mice, with potentially robust levels of activity observed in skeletal muscle:** Our EDO platform exhibited consistently robust activity and acceptable tolerability in a single dose clinical study conducted in healthy volunteers, and in preclinical testing in NHPs under both single and repeat dosing regimens, and in a single dose study in *mdx* mice. For example, in a Phase 1 clinical study of PGN-EDO51, we observed the highest levels of exon skipping and oligonucleotide delivery in humans following a single dose when compared to publicly available data for other exon 51 skipping approaches. In NHP, a dose of 30 mg/kg of PGN-EDO51 achieved over 70% exon 51 skipping in skeletal muscle, including diaphragm, which we believe is the highest rate of exon 51 skipping reported for any approved therapeutic or known development candidate at tolerable target dose levels. In *mdx* mice, we observed the highest level of dystrophin production following a single dose when compared to other clinical-stage DMD therapeutic candidates.
- **Enhanced balance between activity and tolerability, which is designed to afford our platform a wider therapeutic index:** Our delivery peptides have been specifically engineered to achieve a wide therapeutic index, and we have observed robust activity and an improved tolerability profile in NHPs when compared to data published on previous CPPs. In a Phase 1 clinical study, our lead EDO candidate was found to be generally well-tolerated at pharmacologically relevant dose levels. We believe this characteristic is a promising step-change over the narrow therapeutic index observed for previous generations of cell-penetrating peptides.

- **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.
- **Accelerated and 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 our programs, and we envisage that many of our future pipeline opportunities will also leverage our extensive experience with this CPP. 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.

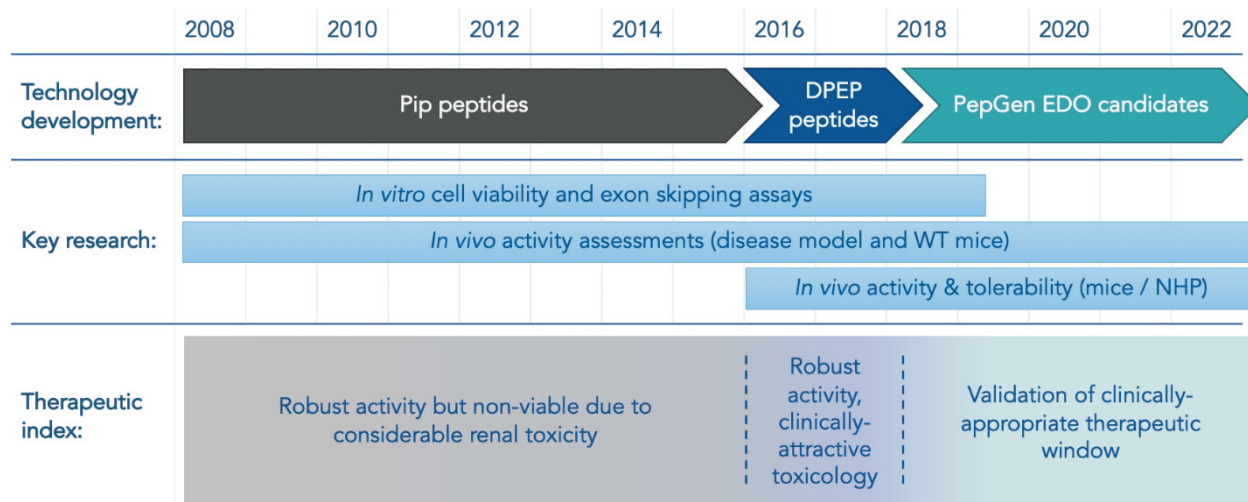
Foundation of Our EDO Platform

A platform built on intelligent design principles and a decade of science

Our EDO peptide platform is the result of over a decade of research conducted in the academic laboratories of our founders Michael Gait, Ph.D. at the Medical Research Council Laboratory of Molecular Biology in Cambridge, UK, and Professor Matthew Wood, M.D., Ph.D. at the University of Oxford. Their pioneering work brought significant advances in CPP technology, moving the field beyond a heavy reliance on arginine residues to drive cellular uptake of oligonucleotide cargos. Together, Gait and Wood developed a new generation of CPPs focused on oligonucleotide delivery, and optimized these peptides for tissue penetration, cellular uptake and nuclear delivery, along with improved tolerability in animal models.

The first generation of Gait and Wood cell-penetrating peptides were termed the ‘Pip’ series. As part of the ongoing collaboration between these two academic groups, a range of Pip-PMO conjugates were screened for their activity both *in vitro* and in the well-established *mdx* mouse model of Duchenne muscular dystrophy. While the Pips exhibited robust activity in preclinical models, they were ultimately determined to be non-viable as therapeutic candidates due to their considerable renal toxicity. However, this early work did provide considerable insight into the structure-activity relationship of this class of molecules.

The poor tolerability profile of the Pips and other early cell-penetrating peptides established a clear need for a step-change in this field. Through an intelligent design process, multiple families of ‘DPEP’ peptides were created to address the limitations associated with previous generations of CPP technology. These novel, unique peptides have overcome the tolerability issues of their predecessors and yet retain the considerable activity of the Pip peptides – a profile that we believe renders the DPEPs well-positioned for therapeutic development. The DPEP peptides underpin our EDO platform, and it is from this portfolio that we have selected and validated the EDO peptide that drives the therapeutic potential of our clinical leads.

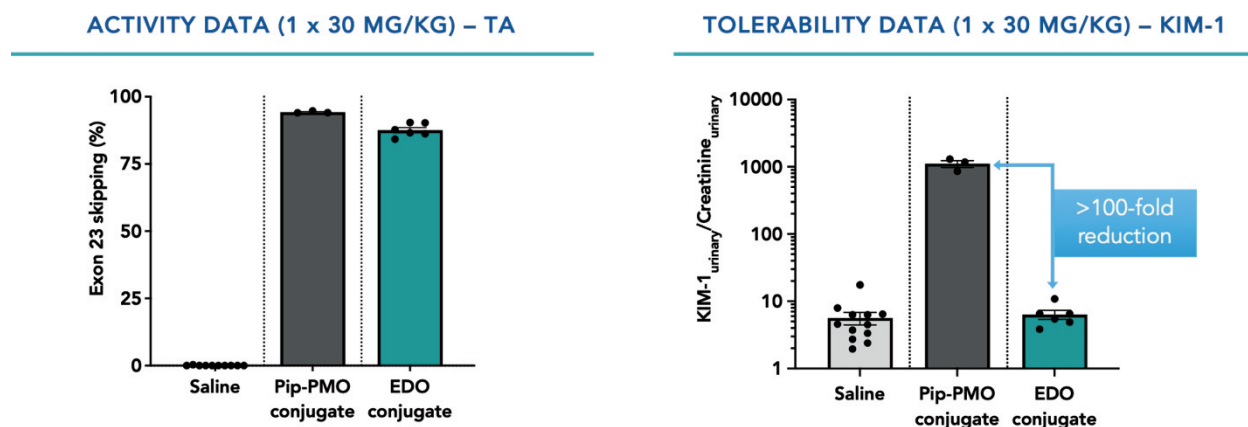


Our EDO technology was developed over more than a decade of research into CPPs.

Comparison with Precursor Technologies

In mouse models, we have observed that our delivery peptides retain the robust activity of previous generations of high arginine content CPPs, and yet possess an improved tolerability profile that we believe increases their likelihood of successful clinical translation. During our extensive preclinical assessments of these novel peptides in murine and NHP models, we have succeeded in efficiently delivering nucleic acid payloads to their targets, and have achieved meaningful levels of activity without the dose-limiting toxicities that have traditionally been associated with other peptides in this class of intracellular delivery agents.

In order to demonstrate that our EDO platform possesses an improved therapeutic index over precursor CPPs – in this instance the ‘Pip’ peptides previously developed by Gait and Wood – we assessed the exon skipping efficiency and tolerability of a number of CPP-PMO conjugates in wild-type mice by utilizing the well-established ASO sequence that skips exon 23 of the murine dystrophin mRNA. As seen in the figure below, we observed in this study that the EDO conjugates retained the high levels of activity seen with the Pip conjugates – over 75% exon skipping was observed in the tibialis anterior, or TA, when measured by RT-PCR following a single dose of 30 mg/kg – while the post-administration urinary levels of Kidney Injury Molecule-1, or KIM-1, a marker of renal toxicity, were reduced by a factor of over 100. Thus, we believe that our EDO technology potentially possesses a wider therapeutic index than these precursor CPPs, which we believe supports the further development and clinical translation of our product candidates and platform.



Our EDO technology has a wider therapeutic index than precursor CPP-PMOs. Graph plotted as mean ± SEM, n = 10 per group for saline control; 3 per group for Pip-PMO conjugate; 6 per group for EDO conjugate.

We believe that this finding represents a true step-change in the CPP field. While traditional CPPs traded activity for tolerability, often because they contained a high absolute number and concentration of arginine residues, our novel delivery peptides are designed to decouple this relationship. We believe the unique structural characteristics of the EDO peptides allow this class of CPPs to retain impressive cell penetration and oligonucleotide delivery while mitigating the unacceptable toxicities seen with earlier generations of CPPs, including the Pips. In driving our pipeline forward, we are seeking to leverage these critical characteristics with the goal of developing a safe and effective portfolio of EDO therapeutics.

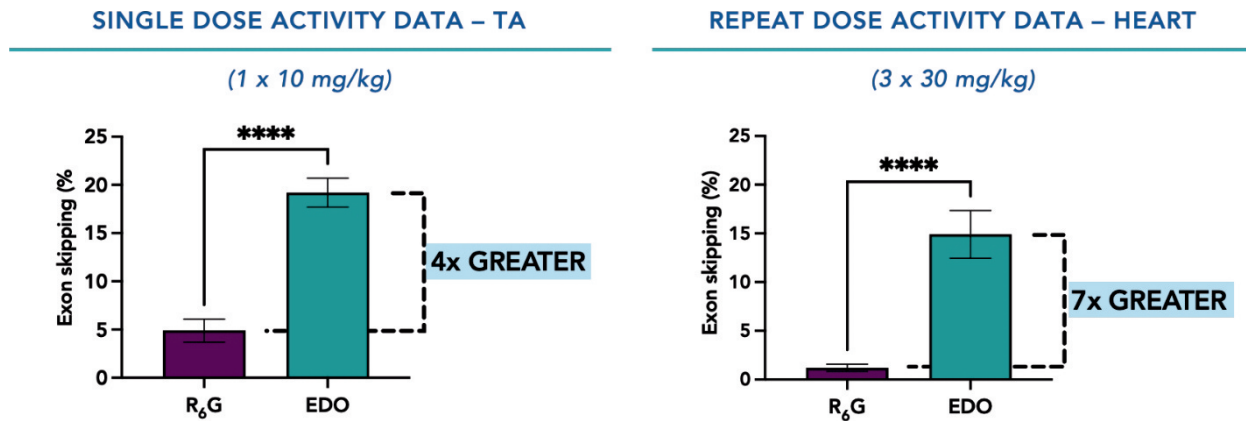
Comparison with Other Oligonucleotide Delivery Technologies in Development

Other CPP-PMO approaches

There are a number of other peptide-mediated approaches that are currently being developed for the delivery of oligonucleotide therapeutics. Of these, we have, through an extensive review of publicly available presentations and patent applications, hypothesized that the most clinically advanced peptide-based delivery approach for oligonucleotides utilizes the cell-penetrating properties of a hexa-arginine sequence with an additional glycine residue. We refer to this CPP as R₆G herein and have conducted extensive head-to-head preclinical studies to compare the biodistribution and activity of our model of this moiety with our novel EDO peptides.

We have observed robust *in vivo* activity of our EDO technology in a number of animal models, with this activity being significantly higher when compared to our model of the competing R₆G approach. In a head-to-head preclinical study conducted in wild-type mice using the established exon 23-skipping antisense oligonucleotide, a single 10 mg/kg intravenous dose of our EDO conjugate resulted in exon skipping levels in the TA that were four-fold higher than those induced by the R₆G conjugate at the same dose when measured by RT-PCR seven days after dosing. In a repeat-dose preclinical study in mice, three 30 mg/kg intravenous doses of our EDO conjugate every two weeks resulted in exon skipping levels in the heart that were seven-fold higher than those of the R₆G conjugate, also dosed three times at 30 mg/kg, when measured by RT-PCR seven days after the last dose. We believe the higher level

of exon skipping achieved in this study supports the ability of our EDO technology to successfully deliver oligonucleotides to cardiac tissue, which in turn provides us with an opportunity to address the primary cause of death in DMD patients.



In preclinical studies, single and multiple doses of our EDO conjugate led to increased exon skipping compared to the R₆G conjugate. Graphs plotted as mean ± SEM; **** denotes extremely significant, $p < 0.0001$; $n = 5$ per group for single dose activity, $n = 8$ per group for repeat dose activity.

Antibody-oligonucleotide approaches

In addition to the CPP-PMO approaches described above, a number of groups are 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, including:

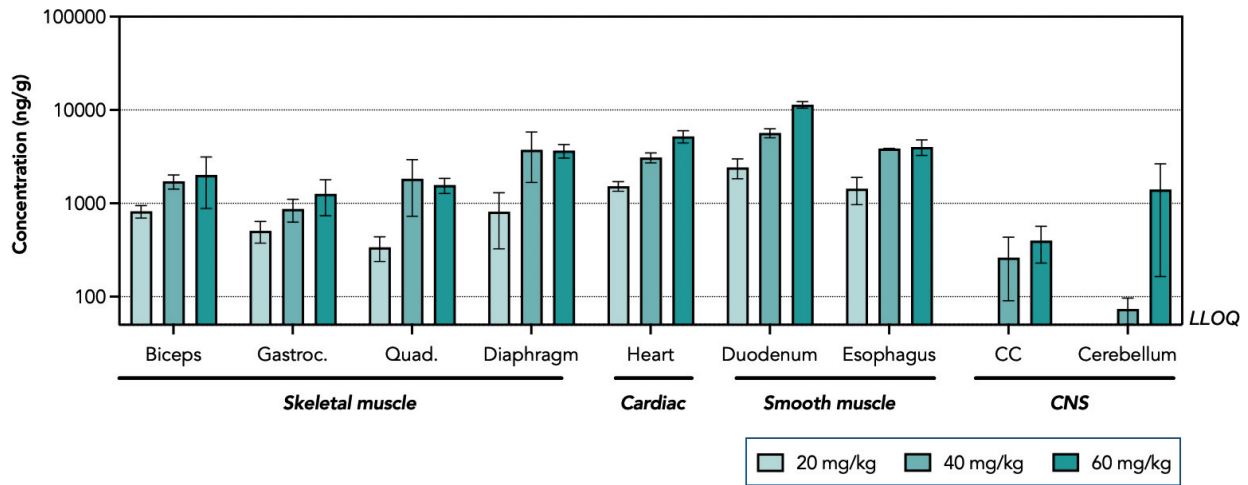
- More efficient tissue penetration due to the small size of our EDO delivery peptides relative to an antibody or antibody fragment;
- The ability to deliver across the blood-brain barrier to the CNS;
- Limited immunogenicity or risk of complement activation due to the considerably lower protein load associated with our EDO peptides; and
- A scalable, facile, fully-synthetic manufacturing process with no cell-based steps that is supported by a readily-characterizable drug product.

We believe these benefits support the further development and clinical translation of our suite of EDO product candidates and underpin our robust competitive position in the neuromuscular and neurologic disease space.

Improved Biodistribution of the EDO platform

We believe that our EDO platform has the potential to achieve robust delivery of cargo therapeutics to a very broad range of target tissues, a characteristic that may provide a critical advantage for our technology in the neuromuscular and neurologic disease space. Following a single intravenous dose of PGN-EDO51 in NHPs, quantifiable levels of PMO were observed in muscle tissues throughout the body one week after administration, including in cardiac muscle, as well as in brain tissues such as cerebral cortex and cerebellum. We believe this broad biodistribution highlights the potential of our technology to deliver to critical yet difficult-to-reach

tissue types like cardiac muscle, and robustly positions our EDO platform in the treatment of diseases with multi-systemic pathologies, like DMD and DM1.

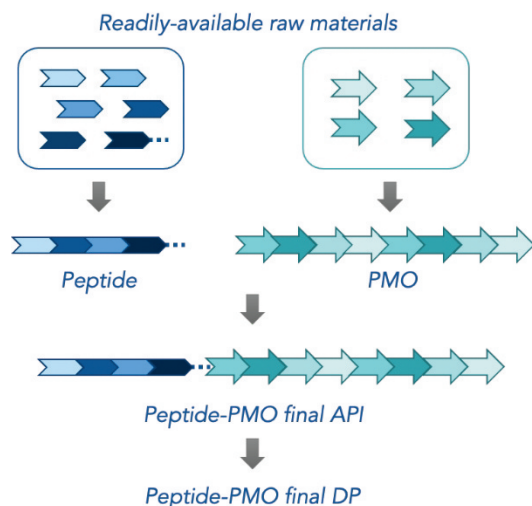


A single administration of PGN-EDO51 in NHPs led to tissue exposure of the cargo PMO therapeutic in muscle and brain tissue one week after dosing. Graph plotted as mean \pm SEM; $n = 2$ per group; CC = cerebral cortex, LLOQ = lower limit of quantification.

Furthermore, we are particularly excited by the potential of this technology to deliver therapeutic agents to the CNS with intravenous dosing. While the levels of the cargo PMO in the cerebral cortex and cerebellum are lower than for the other tissue types investigated, this biodistribution study provides robust evidence to suggest that our peptides are capable of delivering conjugated cargo moieties across the blood-brain barrier, a characteristic which may in turn allow us to address the CNS phenotypes that are evident in DM1 patients. In addition, we believe that this result supports the future development of EDO therapeutics for neurologic indications, and work is ongoing to further understand the ability of our EDO platform technology to deliver cargos to various regions of the brain and CNS.

Scalable Manufacturing Process

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 highly scalable and easily characterizable – attributes that we will seek to leverage to support the rapid development and clinical translation of our EDO conjugate therapeutics. We have produced, manufactured and released multiple cGMP batches, and have successfully utilized this material in a Phase 1 clinical trial.



HIGHLIGHTS:

- **Fully synthetic** manufacturing process; **no cell-based steps**
- Product and intermediates are **readily characterized**
- Research to date suggests product has **robust stability**
- **Multiple cGMP** batches have been **manufactured and released**

We have developed a robust manufacturing process for our EDO product candidates.

Accelerated and Efficient Pipeline Development

Our initial preclinical programs leverage the same EDO peptide to enhance the delivery and cellular and nuclear uptake of oligonucleotide therapeutic candidates. We intend to apply our deep understanding of our EDO platform and current preclinical programs to support the rapid development of additional product candidates for other neuromuscular and neurologic indications. We believe that the ability of our EDO peptides to deliver exon skipping therapeutics to muscle cells, including cardiac muscle cells, is largely independent of the exact sequence of the PMO. Therefore, by leveraging our existing preclinical data and the plug-and-play nature of our EDO platform, we believe that we are well-positioned to rapidly develop additional product candidates with the potential to drive clinically relevant therapeutic outcomes across a wide variety of tissue types. We have observed the validity of this approach with one of our product candidates by moving from concept to completion of an NHP study in less than 18 months.

Our Portfolio: An Initial Focus on Neuromuscular Diseases

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 five programs.

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

PROGRAM	INDICATION TARGET	DISCOVERY	PRECLINICAL	PHASE 1	PHASE 2	REGISTRATIONAL*
PGN-EDO51	Duchenne muscular dystrophy Exon 51					
PGN-EDODM1	Myotonic dystrophy type 1 DMPK					
PGN-EDO53	Duchenne muscular dystrophy Exon 53					
PGN-EDO45	Duchenne muscular dystrophy Exon 45					
PGN-EDO44	Duchenne muscular dystrophy Exon 44					
FUTURE PIPELINE OPPORTUNITIES						
Additional neuromuscular indications						
Neurologic indications						

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. PGN-EDO51 is designed to splice out exon 51 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. In a Phase 1 clinical trial of PGN-EDO51, we observed the highest levels of exon skipping and oligonucleotide in humans following a single dose, when compared to publicly available data for other exon 51 skipping approaches. In wild-type NHP studies, at tolerable doses, we have observed what we believe is the highest rate of exon 51 skipping in skeletal muscles, including diaphragm, based on cross-trial comparisons with publicly available data for any approved therapeutic or known developmental candidate. Furthermore, in head-to-head studies conducted in wild-type NHPs, we found that PGN-EDO51 had greater activity than R₆G-PMO at the same dose level, a comparator compound which we believe to be structurally equivalent to Sarepta’s SRP-5051, the most clinically advanced peptide-ASO conjugate. In the *mdx* mouse model, we observed the highest level of

dystrophin production in skeletal muscle following a single dose of PGN-EDO23, the murine analogue of PGN-EDO51, when compared to other clinical-stage DMD therapeutic candidates. Our Phase 1 clinical trial also indicated that PGN-EDO51 was generally well-tolerated at pharmacologically relevant dose levels. In 2023, we anticipate opening two clinical trials in DMD patients amenable to an exon 51 skipping. CONNECT1-EDO51 is an open-label MAD study to open in Canada in the first half of 2023, with initial dystrophin, exon skipping and safety data anticipated in 2024. CONNECT2-EDO51 is a multinational, randomized, placebo-controlled MAD clinical trial anticipated to open in the second half of 2023, and is designed to potentially support a future accelerated approval pathway.

Disease background and prevalence

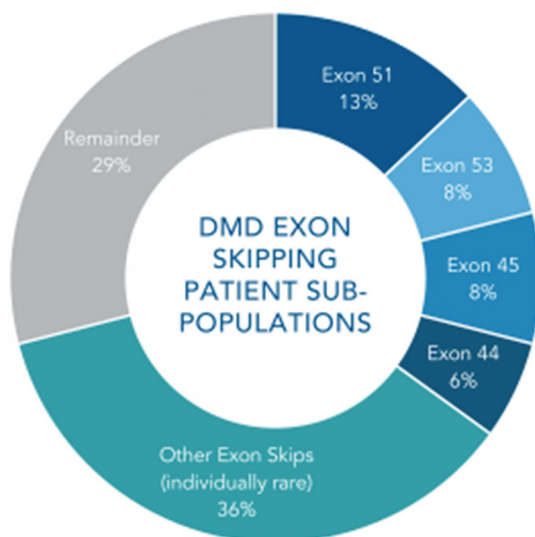
DMD is a debilitating X-linked recessive muscle-wasting disease that predominantly affects boys. It is one of the most prevalent rare genetic diseases globally, with an incidence of up to 1 in 3,500 live male births, and it is invariably fatal by young adulthood. There are up to 15,000 DMD patients in the United States, approximately 25,000 DMD patients in Europe and approximately 5,000 in Japan.

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.

DMD is a progressive disease 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. 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 therapeutic approach, and thus the estimated exon 51 patient population is approximately 2,000 in the United States, 3,200 in Europe and 700 in Japan.



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

Current approaches and limitations

There is no cure for DMD and there are no treatments that have clinically demonstrated a meaningful impact on disease progression. 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. Ataluren is a small molecule that enables the dystrophin protein synthesis machinery to bypass nonsense mutations, where a stop codon is introduced into the dystrophin messenger RNA, or mRNA, thus preventing the synthesis of full-length dystrophin protein. This drug, marketed by PTC Therapeutics, Inc., or PTC as Translarna, has received conditional approval in a number of countries outside of the United States, including across the European Economic Area. However, an approval has yet to be granted by the U.S. Food and Drug Administration, or FDA.

An alternative approach 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 antisense oligonucleotide, or 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.

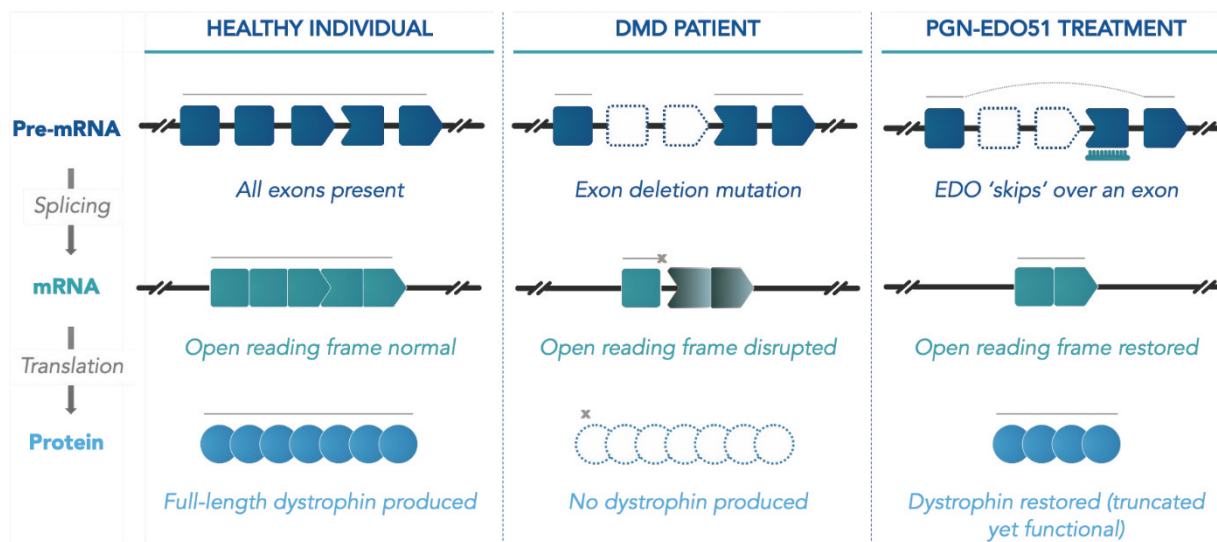
Several unconjugated, or ‘naked’ ASOs have been approved to treat DMD, including eteplirsen, marketed as EXONDYS 51[®] by Sarepta for the treatment of mutations amenable to an exon 51-skipping therapeutic approach. This drug received accelerated approval from the FDA on the basis of an increase of less 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 the European Union, or EU or in Japan on the basis of this minimal degree of dystrophin restoration as a surrogate endpoint.

In addition to oligonucleotide therapeutics, gene therapy approaches are also in clinical development as potential treatments for DMD. For example, Sarepta is developing SRP-9001 in collaboration with Roche for the potential treatment of ambulant patients with DMD and in September 2022 submitted a biologics license application or BLA to the U.S. Food and Drug Administration (FDA) for accelerated marketing approval. 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 ‘microdystrophin’ genes with an unclear functional benefit, where >50% 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:
 - Up to half of all patients possessing antibodies against the most commonly used recombinant AAV vector serotypes, precluding their eligibility for treatment; and
 - Production of anti-AAV antibodies in treated patients, resulting in an inability to re-dose;
- Loss of gene copies over time as patients mature and their cells divide, reducing the durability of therapeutic effect; and
- Complexity and challenges inherent to manufacturing of AAV-based therapies.

Our approach

We are developing a portfolio of 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 activity observed with PGN-EDO51 in the clinic in healthy volunteers and in preclinical models. We believe the higher levels of exon skipping obtained with PGN-EDO51 in healthy volunteers and in NHPs when compared to published and head-to-head data for other such therapies is directly related to the ability of our EDO platform to drive the tissue penetration, cellular uptake and nuclear delivery of the PMO cargo therapeutic to the subcellular compartment where interaction with the mRNA takes place.

Our preclinical data

Activity data: Substantial improvements in exon skipping levels

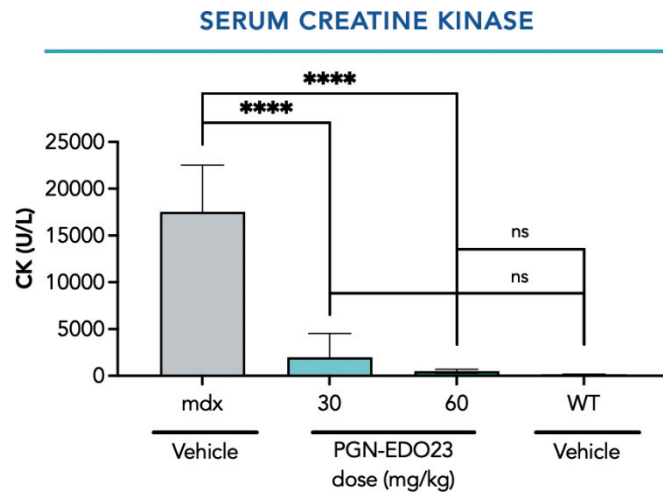
We have evaluated the pharmacology of PGN-EDO51 in a number of *in vitro* and *in vivo* preclinical studies and have observed robust activity in each of the model systems evaluated. In DMD patient cells bearing a deletion of exon 52, where an exon 51-skipping modality restores the open reading frame and facilitates the production of dystrophin, treatment with PGN-EDO51 resulted in high levels of exon 51 skipping across a wide range of concentrations. These results suggest that our first product candidate has the potential to drive robust exon skipping activity in a highly relevant *in vitro* environment and thus supported the advancement of this product candidate to further studies in *in vivo* models.

The *mdx* mouse, a well-characterized model of DMD, has been widely employed in the field to assess the potential activity of therapeutic candidates for this indication. The pathologies evident in the *mdx* mouse model arise due to the presence of a point mutation in exon 23 of the murine dystrophin gene, leading to the production of a dystrophin transcript in which the open reading frame is disrupted. As in DMD patients, this disruption precludes production of a functional dystrophin protein, and as a result *mdx* mice exhibit extensive cell death, fibrosis and muscle tissue degeneration.

We have utilized PGN-EDO23, a murine analogue of PGN-EDO51, to assess the activity of our EDO platform in *mdx* mice. PGN-EDO23 consists of our lead EDO peptide conjugated to the well-established exon 23-skipping PMO, and thus the activity of this compound is highly applicable to PGN-EDO51, and our pipeline candidates PGN-EDO53, PGN-EDO45 and PGN-EDO44.

Creatine kinase, or CK, is a critical biomarker of muscle damage, with this enzyme being elevated in DMD patients from birth. In the absence of dystrophin, the structural integrity of the sarcolemma, or muscle cell membrane, is disrupted, leading to the release of CK into the blood. Following intravenous administration of a single, generally well-tolerated dose of 30 mg/kg or 60 mg/kg of PGN-EDO23, we observed normalization of serum CK to wild-type levels in *mdx* mice seven days post-dose. The normalization of CK levels observed in this study suggest that PGN-EDO23 may restore muscle cell integrity and prevent further damage in *mdx* mice.

under a single dose regimen, and we believe that this outcome supports the potential therapeutic utility of PGN-EDO51 in the treatment of DMD patients.



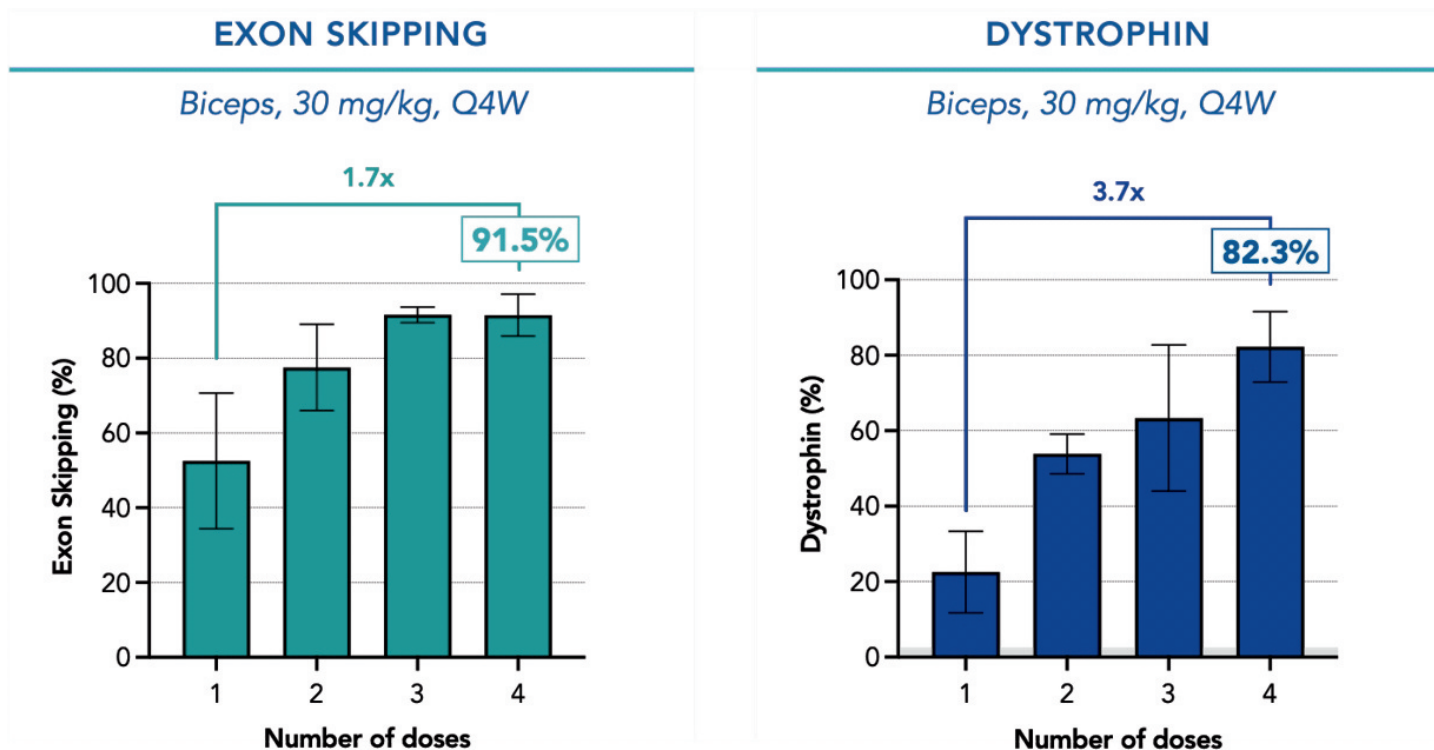
A single dose of PGN-EDO23, the murine analogue of PGN-EDO51, was observed to normalize creatine kinase, a marker of muscle damage in *mdx* mice. Graph plotted as mean ± SEM; **** = $p \leq 0.0001$, ns = $p \geq 0.05$; $n = 3$ for control groups, $n = 5$ for treated group.

In addition to this significant reduction in CK, we also observed high levels of exon 23 skipping and dystrophin production in *mdx* mice when measured by RT-PCR and Western blot, respectively, seven days after a single dose of PGN-EDO23. In the quadriceps, a single, generally well-tolerated dose of 60 mg/kg yielded an exon skipping rate of 86.3% and dystrophin restoration to 90.4% of wild-type levels, while in the biceps the same dose resulted in 93.1% exon skipping and 99.7% dystrophin restoration. In the diaphragm, this dosing regimen afforded an exon skipping rate of 76.6% and dystrophin restoration levels of 80.6%, and in the critical cardiac tissues the exon skipping rate was observed to be 62.3%, with dystrophin restoration levels of 25.7%.

We subsequently conducted a repeat-dose study where 30 mg/kg of PGN-EDO23 was intravenously administered to *mdx* mice once, twice, three or four times every four weeks, with tissue collection and analysis four weeks following the final dose. In the biceps, the level of exon 23 skipping was observed to be 91.5% after four doses when measured by RT-PCR, a value that was 1.7 times higher than that observed following a single dose. Dystrophin production was measured by western blot, and was observed to reach a level of 82.3% in the same tissue after four doses. In comparison, a level of 22.5% was 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 four-weekly dosing regimen for PGN-EDO51, and serves to highlight our belief that dystrophin production is likely to increase with subsequent doses in DMD patients.

Given the relevance of the *mdx* mouse as a preclinical model for DMD, we believe that these robust exon skipping and dystrophin readouts are supportive of the potential activity of the EDO platform in this disease and the potential clinical benefit we may deliver to patients with our lead candidate, if approved. In addition, the levels of dystrophin production we observed in *mdx*

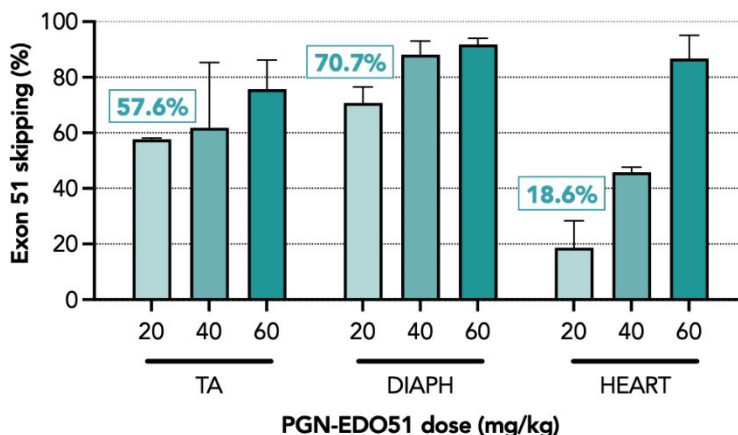
skeletal muscles were higher than the levels obtained by other clinical-stage DMD therapeutic candidates, with this cross-trial comparison further highlighting what we believe to be the potentially best-in-class nature of our approach.



Robust exon skipping and dystrophin restoration was observed with repeat dosing of PGN-EDO23 in *mdx* mice. Graph plotted as mean \pm SD; n = 4-5 for each group; grey band represents dystrophin LLOQ (2.5%).

We have 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.

In a preclinical intravenous dose study, we observed that a single administration of PGN-EDO51 in NHPs led to high rates of exon 51 skipping in the TA, diaphragm and heart, with these tissues being harvested seven days post-dose and then assayed using a RT-PCR protocol. Of particular note are the results obtained for the heart, where exon skipping rates of 18.6%, 45.8% and 86.7% were observed following single doses of 20, 40 and 60 mg/kg respectively. In the TA, exon skipping levels of 57.6% were observed following a single dose of 20 mg/kg, while the diaphragm yielded levels of 70.7% at the same dose. We believe the results obtained in this study for PGN-EDO51 represent the highest rate of exon 51 skipping in primate skeletal muscles, including diaphragm, following a single administration at tolerable target dose levels of any approved therapeutic or known development candidate.



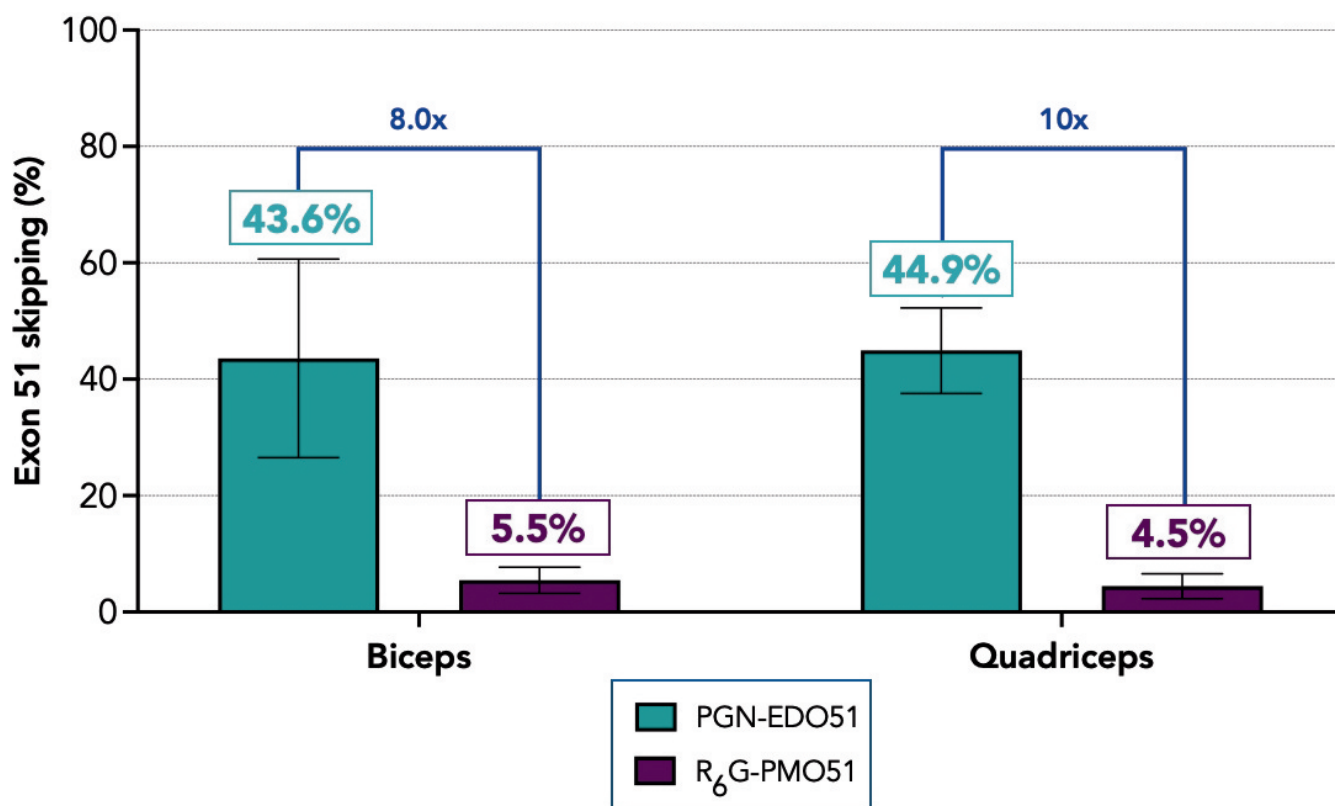
Single doses of PGN-EDO51 led to high rates of exon 51 skipping in a preclinical NHP study. Graph plotted as mean \pm SEM; $n = 2$ per group.

In order to benchmark the ability of our lead EDO peptide to improve the tissue penetration, cellular uptake and nuclear delivery of oligonucleotide therapeutics, we carried out a study comparing our EDO-conjugated PMO to an R6G peptide conjugated to the same PMO. We have conducted a considerable number of benchmarking studies of PGN-EDO51 against this conjugate, and we believe – based on publicly-available information – that R6G-PMO is structurally equivalent to SRP-5051, Sarepta’s CPP-PMO product candidate that is currently in clinical development for the treatment of DMD patients who are amenable to an exon 51-skipping approach. In this preclinical study, NHPs were dosed intravenously with either PGN-EDO51, R6G-PMO or a saline control three times with an interval of two weeks between doses. Biopsies of the biceps and quadriceps were collected seven days after the first and second dose, and tissues were harvested seven days after the final dose.

Through RT-PCR analysis of key skeletal muscles collected by biopsy seven days after the first dose, we observed markedly higher exon skipping levels for PGN-EDO51 when compared to R6G-PMO. At 30 mg/kg, a single dose of PGN-EDO51 afforded an exon 51 skipping level of 43.6% in the biceps, which was 7.9 times higher than the level of 5.5% observed for R6G-PMO. In the quadriceps, this differential was 10 times, with 44.9% exon 51 skipping observed for PGN-EDO51, and just 4.5% for R6G-PMO.

EXON SKIPPING

30 mg/kg



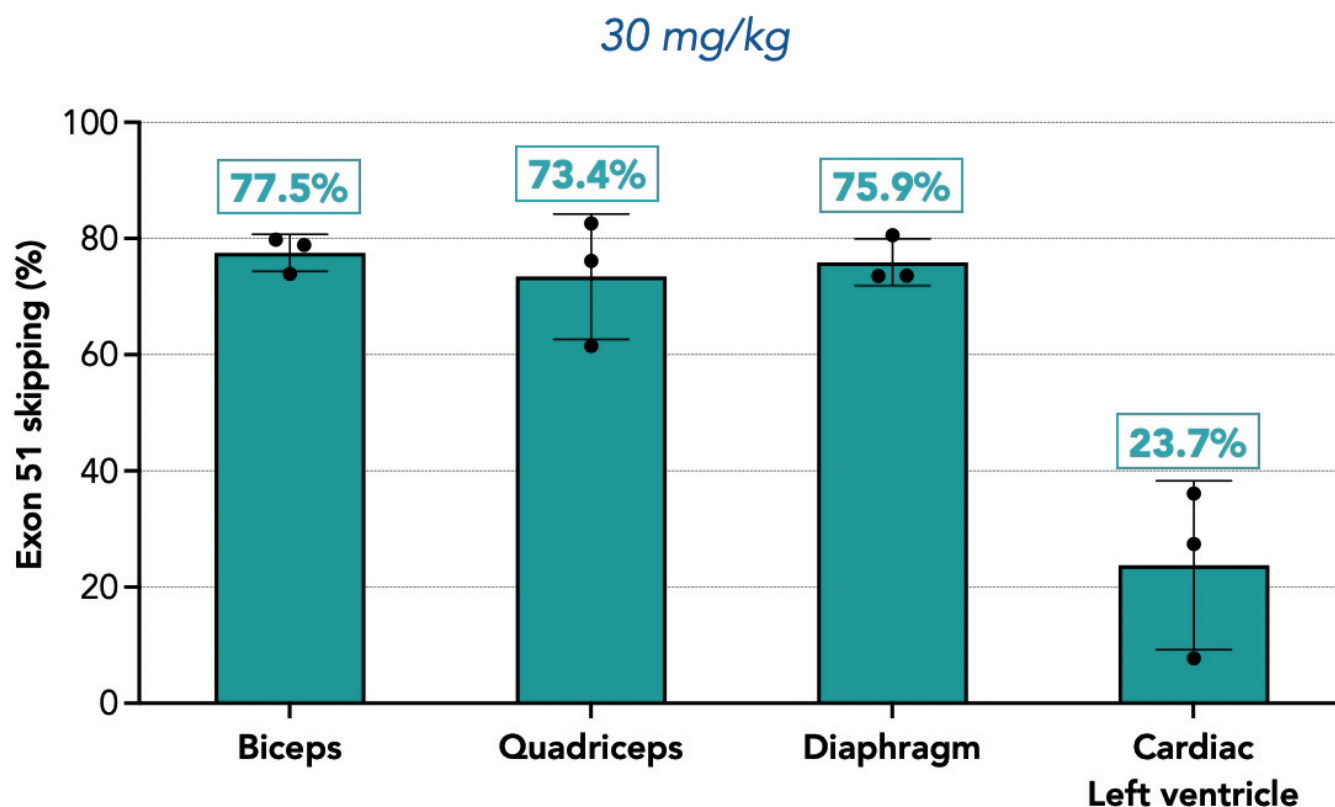
Single dose administration of PGN-EDO51 yielded considerably higher exon skipping levels than R₆G-PMO. Graph plotted as mean \pm SD; $n = 3$ per group; study was not powered for statistical significance.

Following three bi-weekly doses of 30 mg/kg, we observed robust exon skipping activity for PGN-EDO51, with levels of greater than 70% obtained in key skeletal muscles following analysis by RT-PCR seven days after the final dose. In biceps, an exon 51 skipping level of 77.5% was obtained; and in quadriceps, 73.4%. In patients with DMD, cardiomyopathy and subsequent heart failure is a leading cause of death, and predominantly involves the left ventricle, the chamber responsible for pumping oxygenated blood around the body. In addition to these cardiac pathologies, DMD patients also experience a progressive impairment in pulmonary

function due to the impact of the dystrophic process on the respiratory muscles, including the diaphragm, which in turn results in significant morbidity and mortality over time. We observed 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 our lead candidate to address the key pathologies that are evident in DMD.

In addition to cardiac pathologies, DMD patients also experience a progressive impairment in pulmonary function due to the impact of the dystrophic process on the respiratory muscles, including the diaphragm, which in turn results in significant morbidity and mortality over time. In the critical diaphragm tissue, a 10 mg/kg repeat dose of PGN-EDO51 afforded exon skipping rates in NHPs that were approximately 12-fold higher than those observed for R₆G-PMO. No serious adverse events were observed during this study.

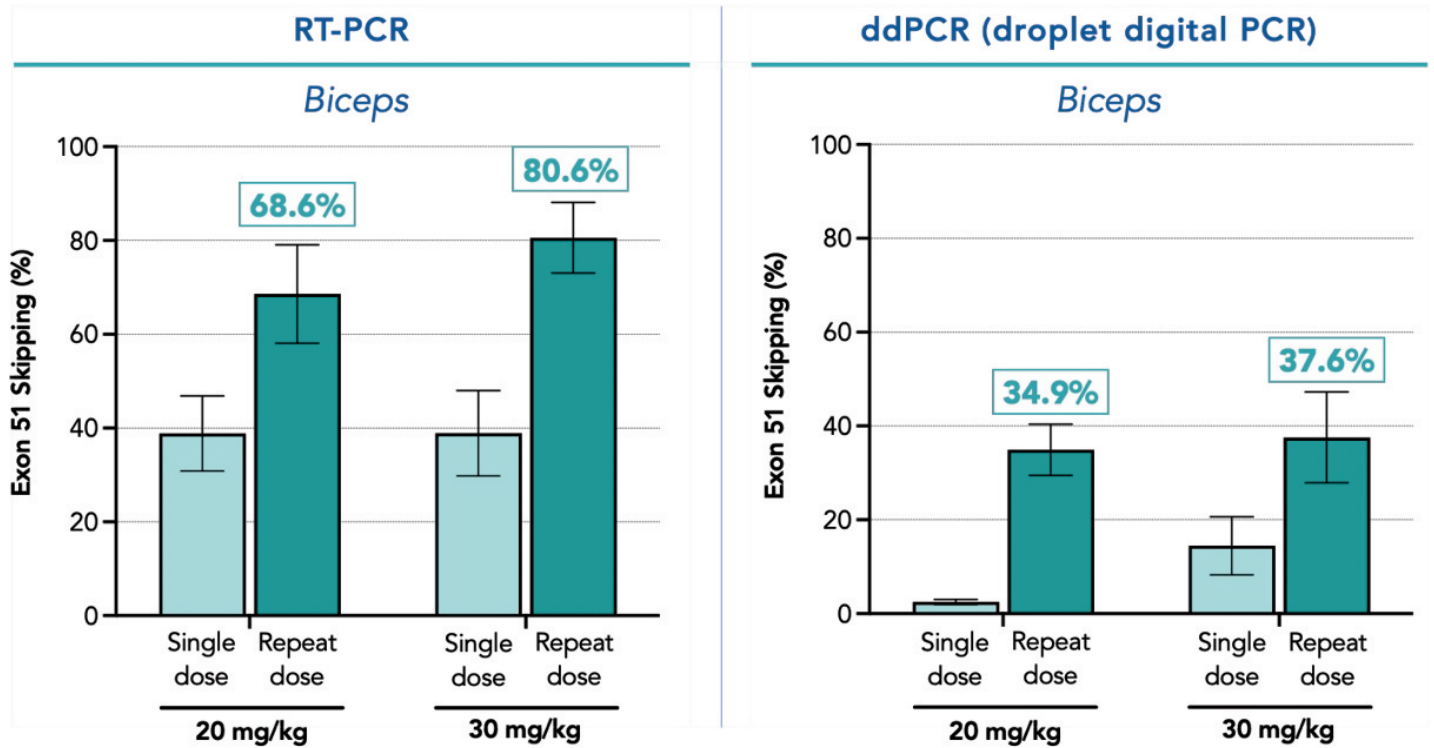
EXON SKIPPING



Preclinical repeat dose administration of PGN-EDO51 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.

In order to understand the potential accumulation of exon 51-skipped transcripts under a four-weekly, or Q4W, repeat dose regimen, we assessed NHP tissue samples of the biceps collected seven days following a single administration of PGN-EDO51, and compared these with samples of the biceps collected seven days following four administrations of PGN-EDO51 every four weeks. The levels of exon 51 skipping of the *DMD* transcript were assayed via an RT-PCR protocol and a droplet digital PCR, or ddPCR, protocol. The results obtained showed a robust accumulation in the levels of the exon 51 skipped transcript between one dose and four doses under both PCR protocols. Following four doses of 20 and 30 mg/kg, exon 51 skipping levels were measured by RT-PCR to be 68.6% and 80.6% respectively, with these levels being 1.8 times and 2.1 times higher than for a single dose. Under a ddPCR assay, these levels were 34.9% and 37.6% following four doses at 20 and 30 mg/kg respectively, which were 14 times and 2.6 times

higher than for a single dose. We believe this accumulative effect suggests that the activity of PGN-EDO51 is likely to increase with chronic dosing in DMD patients, which further supports the clinical potential of our lead candidate in this devastating disease.

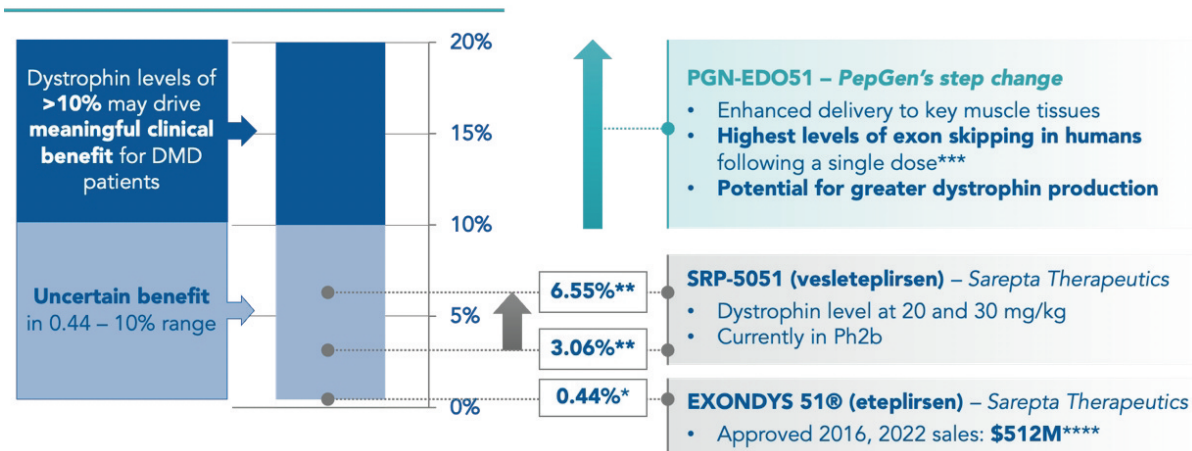


Exon skipped transcripts in the biceps accumulated under a preclinical repeat-dose regimen of PGN-EDO51 when assessed by RT-PCR and ddPCR. Graph plotted as mean \pm SD; $n = 3-8$ per group; study was not powered for statistical significance.

To provide context to our NHP data, we believe it is important to consider data presented by Sarepta for SRP-5051, which we understand to be structurally equivalent to the R₆G-PMO conjugate we used as a comparator in our preclinical studies. In a Phase 2 clinical trial of SRP-5051 in DMD patients amenable to an exon 51-skipping approach, Sarepta reported that patients treated with 30 mg/kg of their candidate achieved dystrophin production of 6.55% of normal levels. A dose response was observed in this trial, with patients dosed at 30 mg/kg achieving twice as much dystrophin production as patients treated with 20 mg/kg. A positive relationship was observed between exon skipping levels and dystrophin expression, with higher exon skipping resulting in higher dystrophin expression.

In our head-to-head study in NHPs, PGN-EDO51 dosed at 10 mg/kg resulted in near equivalent exon skipping to the 30 mg/kg dose of R₆G-PMO, and PGN-EDO51 dosed at 30 mg/kg resulted in significantly higher exon skipping than R₆G-PMO at the same dose. Given these results, we believe that PGN-EDO51 at the 10 mg/kg dose has the potential to afford comparable dystrophin levels to those obtained following treatment with SRP-5051 at the 30 mg/kg dose in DMD patients. We believe that doses of PGN-EDO51 above 10 mg/kg could generate even greater dystrophin than obtained for the 30 mg/kg dose of SRP-5051, which may lead to clinically meaningful outcomes for those suffering from this disease. Due to the long half-life of the dystrophin protein, and the accumulation in exon skipping that we observed during our repeat-dose study, we believe that these levels could continue to accumulate over time and thus further enhance the clinical benefit afforded to DMD patients by our EDO technology.

DYSTROPHIN PRODUCTION (%)



PGN-EDO51 was observed to generate greater dystrophin than SRP-5051 in NHPs supporting its potential in DMD patients.*

*Clinical data included in drug label (FDA). **Source: Sarepta MOMENTUM study update, 20 and 30 mg/kg cohort, 03May21.

*** Comparative statements are based on cross-trial comparisons with publicly-available data for other exon skipping approaches that have been assessed following a single dose. **** Source: Sarepta 2022 10-K filing.

In addition to Sarepta's competing SRP-5051 approach, several organizations focused on the development of next-generation oligonucleotide therapeutics have released NHP exon skipping data. Dyne, a clinical-stage company utilizing an antigen-binding fragment, or Fab, as a delivery vector for nucleic acid species, announced NHP data in the fourth quarter of 2021 for DYNE-251, their lead product candidate for the treatment of DMD patients amenable to an exon 51-skipping approach. Following two bi-weekly or four weekly doses of 30 mg/kg, with tissue analysis two weeks or one week, respectively, after the final dose, Dyne reported very minimal levels of exon skipping in quadriceps, diaphragm and whole heart. An administration regimen of five weekly doses of 30 mg/kg, with tissue analysis four weeks after the final dose, yielded more robust results: 18% exon 51 skipping in quadriceps, 52% in diaphragm and 43% in whole heart. While this data was not obtained as part of a head-to-head comparison, we reported exon 51-skipping levels of 73.4% in the quadriceps and 75.9% in the diaphragm following a dosing regimen of three bi-weekly doses of 30 mg/kg of PGN-EDO51 with tissue analysis one week after the final dose, and 18.6% in whole heart and 70.7% in diaphragm following a single dose of 20 mg/kg of PGN-EDO51 with tissue analysis one week after dosing. These NHP results serve to further cement our belief that PGN-EDO51 has the potential to address multiple, critical muscle types in this competitive space.

We are additionally aware of other cell-penetrating peptide and antibody-conjugated approaches in development for the treatment of DMD patients amenable to exon 44- and exon 45-skipping therapeutic approaches.

Preclinical tolerability data: Generally well-tolerated through clinically relevant dose levels

PGN-EDO51 was generally well-tolerated in single-dose, 28-day Good Laboratory Practice, or GLP, toxicity studies in mice and NHPs; no treatment-related mortality and no serious adverse events were observed through the therapeutic dose range. There were no adverse microscopic observations and no adverse impacts on clinical chemistry markers at clinically relevant dose levels.

An *in vitro* T cell stimulation assay conducted with peripheral blood mononuclear cells from healthy donors indicated that PGN-EDO51 has a very low immunotoxicity risk. This is further supported by data showing that the pharmacokinetic profile of PGN-EDO51 was similar following the first and third dose, suggesting no significant neutralizing anti-drug antibody responses were present after a three-dose regimen in NHPs.

We submitted our preclinical dataset for PGN-EDO51, including both pharmacology and toxicity studies, to Health Canada as part of our CTA filing in the first quarter of 2022. Upon review, Health Canada subsequently authorized our CTA.

Clinical development

Phase 1 healthy volunteer study: highest levels of exon skipping and oligonucleotide delivery in humans following a single dose

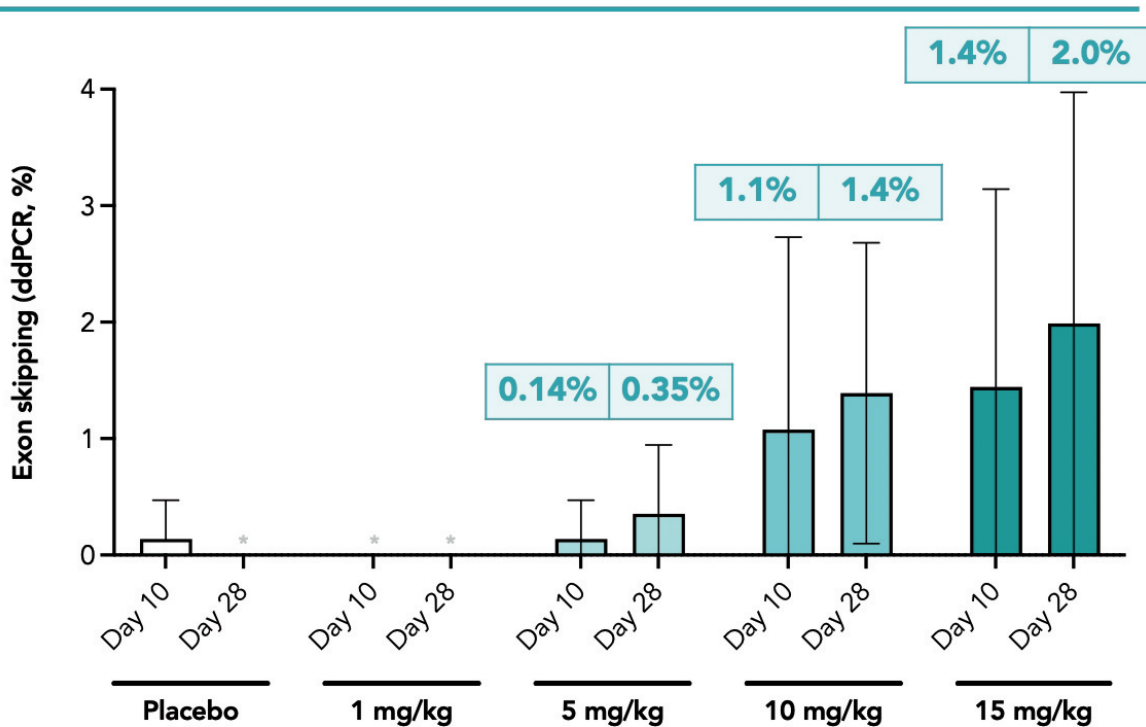
In the third quarter of 2022, we completed a first-in-human, Phase 1, single-center, randomized, double-blind, placebo-controlled, single ascending dose clinical trial to assess the target engagement (exon skipping), pharmacokinetics (oligonucleotide tissue concentration), safety and, tolerability of 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 droplet digital PCR, or ddPCR, assay.

Target engagement (exon skipping in biceps): A dose dependent increase in exon skipping was observed in biceps, with the levels obtained being the highest observed in humans following a single dose, based on cross-trial comparisons with publicly available data for other exon 51 skipping approaches.

- In the 10 mg/kg dose cohort, PGN-EDO51 exhibited mean exon skipping of 1.1% and 1.4% in biceps biopsies taken at Day 10 (n=6) and Day 28 (n=6), respectively;
- In the 15 mg/kg dose cohort, PGN-EDO51 exhibited mean exon skipping of 1.4% and 2.0% in biceps biopsies taken at Day 10 (n=5) and Day 28 (n=6), respectively.

EXON SKIPPING (BICEPS)

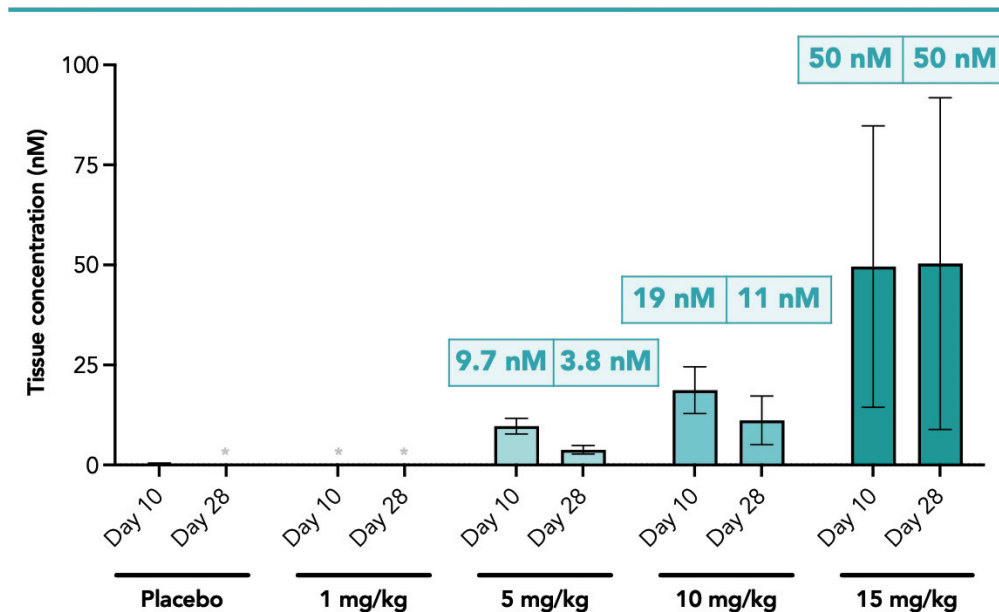


We observed the highest levels of exon skipping in humans following a single dose based on cross-trial comparisons with publicly available data for other exon 51 skipping approaches. Data is shown as mean \pm SD; n = 6 for PGN-EDO51 (n = 5 for D10 at 15 mg/kg), n = 8 for placebo. Asterisks indicate values that were under the lower level of quantification.

Pharmacokinetics (tissue concentration in biceps); A dose-dependent increase in PGN-EDO51 tissue concentration was observed in biceps, with the levels obtained being the highest observed in humans for a DMD therapeutic following a single dose, based on cross-trial comparisons with publicly available data for other exon 51 skipping approaches.

- In the 10 mg/kg dose cohort, PGN-EDO51 exhibited mean oligonucleotide tissue concentrations of 19 nM and 11 nM in biceps biopsies taken at Day 10 (n=6) and Day 28 (n=6), respectively;
- In the 15 mg/kg dose cohort, PGN-EDO51 exhibited mean oligonucleotide tissue concentrations of 50 nM and 50 nM in biceps biopsies taken at Day 10 (n=5) and Day 28 (n=6), respectively.

TISSUE CONCENTRATION (BICEPS)



High, persistent tissue concentrations of oligonucleotide were observed. Data is shown as mean \pm SD; $n = 6$ for PGN-EDO51 ($n = 5$ for D10 at 15 mg/kg), $n = 8$ for placebo. Asterixis indicate values that were under the lower level of quantification.

We believe that the exon skipping and tissue concentration 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. Furthermore, Sarepta’s recent clinical trials of SRP-5051 provide a relevant benchmark with regards to exon skipping target engagement in healthy adults. We note here that, in a single dose trial in HV, administration of SRP-5051 resulted in median exon skipping levels of $<0.2\%$. However, in a subsequent multiple ascending dose trial in DMD patients, treatment with SRP-5051 yielded exon skipping levels that were multiple times higher at the same dose level. Thus, based on this precedent, we anticipate that the exon skipping rates afforded by PGN-EDO51 when administered to patients have the potential to exceed the rates when administered to HVs.

Safety and tolerability: The trial met its primary endpoint, providing evidence that PGN-EDO51 was generally well tolerated at clinically relevant doses. 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, were assessed as mild and resolved without any intervention;
- Serum cystatin C, the recommended biomarker to assess renal function in DMD, did not change;
- There was no evidence of hypomagnesemia.

There were transient, reversible changes in kidney biomarkers that resolved without intervention at higher doses. 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. Transient mild (Grade 1) to moderate (Grade 2) hypomagnesemia was observed in two participants at the 15 mg/kg dose and did not require any intervention. Under this Phase 1 protocol 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 oligo levels and exon skipping levels in muscle observed at 5 mg/kg and 10 mg/kg, further dose escalation was not deemed necessary by the sponsor.

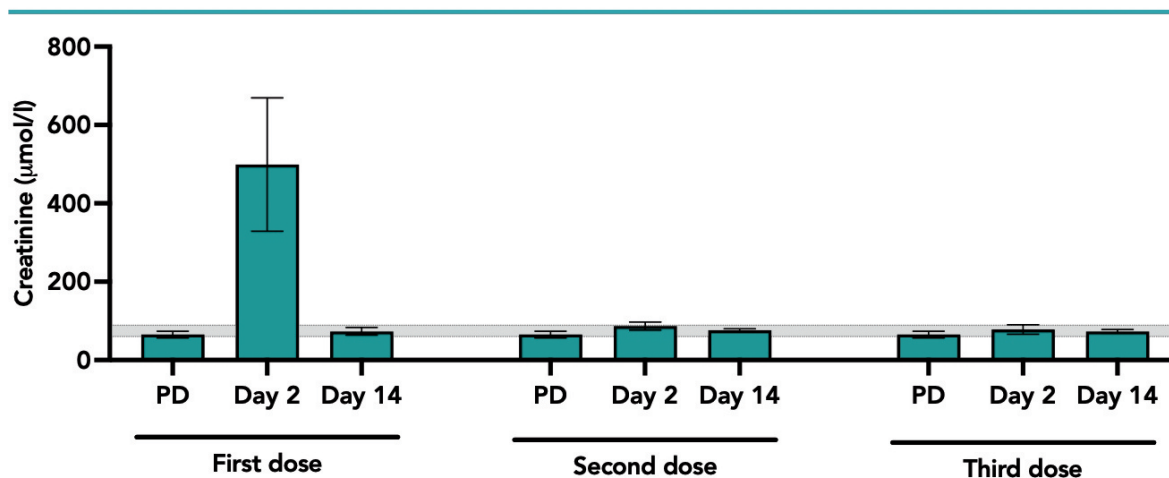
TEAEs were mild and resolved without intervention at clinically relevant doses. Asterix denotes that no Grade 4 or 5 TEAEs were recorded.

PH1 TRIAL SAFETY & TOLERABILITY SUMMARY

Healthy Volunteers (HV) with ≥ 1 AE, n (%)	Placebo (n=8)	Cohort A: 1 mg/kg (n=6)	Cohort B: 5 mg/kg (n=6)	Cohort C: 10mg/kg (n=6)	Cohort D: 15 mg/kg (n=6)	PGN-EDO51 Total (n=24)
Any AE	4 (50)	4 (66.7)	2 (33.3)	5 (83.3)	6 (100)	17 (70.8)
Related to study drug	1 (12.5)	2 (33.3)	0	4 (66.7)	6 (100)	12 (50)
Serious AE related to study drug	0	0	0	0	1 (16.7)	1 (4.2)
AE leading to discontinuation	0	0	0	0	0	0
AE leading to death	0	0	0	0	0	0
Number of Related TEAEs by CTCAE v5.0 grading*						
Grade 1 (Mild)	1	1	0	7	12	20
Grade 2 (Moderate)	0	1	0	0	3	4
Grade 3 (Severe)	0	0	0	0	1	1

In prior multiple ascending dose NHP studies, we observed that kidney biomarker elevations were reduced with subsequent administrations, a finding that supports the potential tolerability of PGN-EDO51 with repeat dosing. In one such study, three doses of PGN-EDO51 were administered intravenously to NHP over 30 minutes every second week, and serum chemistry markers were assessed 2 days and 14 days after each dose. Following the first administration, an elevation in key kidney biomarkers was observed at Day 2; this elevation was completely resolved by Day 14. Following the second and third administrations, the Day 2 elevations seen previously were ameliorated, and we believe it to be likely that this attenuation in acute kidney biomarker elevations may also be observed in human clinical trial participants under a repeat-dose regimen.

REPEAT-DOSE SERUM CREATININE LEVELS (HIGH-DOSE COHORT)



In NHP, an amelioration of elevations in kidney biomarkers was observed with repeat dosing of PGN-EDO51. Graph plotted as mean \pm SD; n = 3 per group; grey bar shows normal range.





Sarepta noted that hypomagnesemia, a condition in which there is a low level of magnesium in the body, was observed in DMD patients at a dose levels of 10, 20 and 30 mg/kg of SRP-5051 in their repeat-dose clinical trials, an observation that is consistent with our own findings in repeat-dose preclinical testing of R₆G-PMO. We have also observed hypomagnesemia as a side effect of PGN-EDO51 at doses above the therapeutic range, both in healthy volunteers following a single dose of 15 mg/kg, and in NHPs following multiple administrations.

Sarepta has initiated what it reports could be the pivotal trial for SRP-5051, with a protocol that includes magnesium supplementation. Sarepta has further noted that this modulation in clinical chemistry may be reversible, monitorable and manageable with prophylactic oral administration of such supplements. Based on these findings, we anticipate that we may also observe hypomagnesemia following repeat-dose administration of PGN-EDO51 in our patient clinical trials. We intend to carefully monitor serum magnesium levels in our upcoming Phase 2 patient clinical trials.

Phase 2 MAD studies in exon 51 skipping-amenable DMD patients

The readouts obtained from our Phase 1 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 trial of PGN-EDO51 in patients. Based on these inputs, we have designed what we believe to be an efficient and informative clinical path to evaluate 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-EDO51, to be conducted in Canada and a larger, global, randomized, double-blind placebo-controlled MAD study, CONNECT2-EDO51. We anticipate opening CONNECT1-EDO51 in the first half of 2023, with initial dystrophin, exon skipping and safety data in 2024. CONNECT2-EDO51 is expected to open in the second half of 2023, and will potentially be a registrational trial, subject to alignment with regulatory authorities.

 <p>CONNECT1-EDO51 Ph2 open-label MAD study in patients (<i>planned initiation 1H23</i>) ➤ Initial dystrophin, exon skipping and safety data anticipated in 2024</p>	 <p>Connect 1 EDO51</p>	<p>Dystrophin, exon skipping and safety data anticipated in 2024</p>
 <p>CONNECT2-EDO51 Ph2 randomized, double-blind, placebo-controlled MAD study in patients (<i>planned initiation 2H23</i>) • Potential to support accelerated approval</p>	 <p>Connect 2 EDO51</p>	<ul style="list-style-type: none"> • Preclinical data suggests Q4W repeat dosing has the potential to drive meaningful clinical benefit in individuals with DMD • Studies to be conducted in parallel • Designed to provide potential path to accelerated approval

Our Phase 2 clinical development plan for PGN-EDO51 is designed to support a potential accelerated approval pathway.

We believe that this clinical path may enable us to pursue an accelerated approval pathway for PGN-EDO51 with the FDA. A product candidate may 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 and is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit. In the DMD space, the FDA has approved four drugs under the accelerated approval pathway since 2016. If we receive positive results from our Phase 2 trials for PGN-EDO51 that show an acceptable 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 discussions with the FDA for an accelerated approval pathway.

Four drugs have received accelerated approval in DMD to date.

Drug	Approval	Sponsor	Population	Sample size	Placebo Dystrophin	Drug Dystrophin
EXONDYS 51® (eteplirsen)	2016	Sarepta Therapeutics	Exon 51	12	n/a	0.44%
VYONDYS 53® (golodirsen)	2019	Sarepta Therapeutics	Exon 53	12	n/a	1.02%
VILTEPSO® (viltolarsen)	2020	NS Pharma	Exon 53	8	n/a	5.90%
AMONDYS 45® (casimersen)	2021	Sarepta Therapeutics	Exon 45	43	0.76%	1.74%

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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 cytosine-uracil-guanine, or CUG, trinucleotide repeat expansion present in the *DMPK* mRNA, thus reducing the ability of these trinucleotide repeats to sequester 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 *ex vivo*, we observed that treatment with PGN-EDODM1 led to the robust correction of multiple downstream mis-spliced transcripts and a reduction in toxic nuclear foci. In our *in vivo* preclinical studies, a single dose of PGN-EDODM1 was observed to correct the molecular and functional phenotypes presented in the human skeletal actin – long repeat, or HSA^{LR}, mouse model of disease, ameliorating downstream mis-splicing events, reversing myotonia and normalizing mobility. We also observed that the molecular correction effected by PGN-EDODM1 in this preclinical mouse model exhibited a durability of effect that was in excess of six months. Furthermore, the tissue concentrations of oligonucleotide that were found to be pharmacologically active in the HSA^{LR} mouse model were similar to those observed for PGN-EDO51 in human muscle in a Phase 1 clinical trial, supporting the ability of PGN-EDODM1 to achieve potentially therapeutic levels of oligonucleotide in the clinic. We anticipate opening a single ascending dose clinical trial of PGN-EDODM1, FREEDOM-DM1 in DM1 patients in the first half of 2023, with functional assessments, correction of mis-splicing and safety data expected in 2024.

Disease background and prevalence

DM1 is a monogenic, autosomal dominant, progressive disorder that primarily affects skeletal, cardiac and smooth muscles, with 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 United States, 75,000 patients in Europe and 15,000 patients in Japan. However, under- and mis-diagnosis 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; cardiac pathologies; 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 myotonic dystrophy protein kinase, or *DMPK*, gene. Specifically, DM1 is caused by an expansion in the number of cytosine-thymine-guanine, or 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:

- **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 *DMPK* 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 have muscle weakness and cardiac arrhythmia, with an average lifespan of 48 years 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. There are a number of therapeutics currently in clinical development for the treatment of DM1 symptoms, including the small molecules tideglusib and ERX-963. However, neither of these therapeutics treat the underlying cause of disease, and thus we believe that a considerable unmet need will remain in DM1 even if these therapies are approved. 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 tissue 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 monoclonal antibodies, or mAbs, and antigen-binding fragments, or Fabs, that target the transferrin receptor 1, or TfR1, in order to deliver cargo oligonucleotides. In contrast to our mechanism of action, where MBNL1-*DMPK* transcript binding is disrupted, these AOCs are designed to knockdown *DMPK* as a therapeutic modality. However, such knockdown or degradation approaches that cannot differentiate between expanded and non-expanded transcripts may risk confounding effects due to 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. This condition can be created artificially by the degradation of RNA levels to such an extent that there is no longer sufficient protein produced 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.

We believe that PGN-EDODM1 has the potential to offer a number of benefits when compared to these alternative technologies, as outlined in the table below:

Our approach is differentiated against competing AOC *DPMK* knockdown therapeutics in development for DM1.

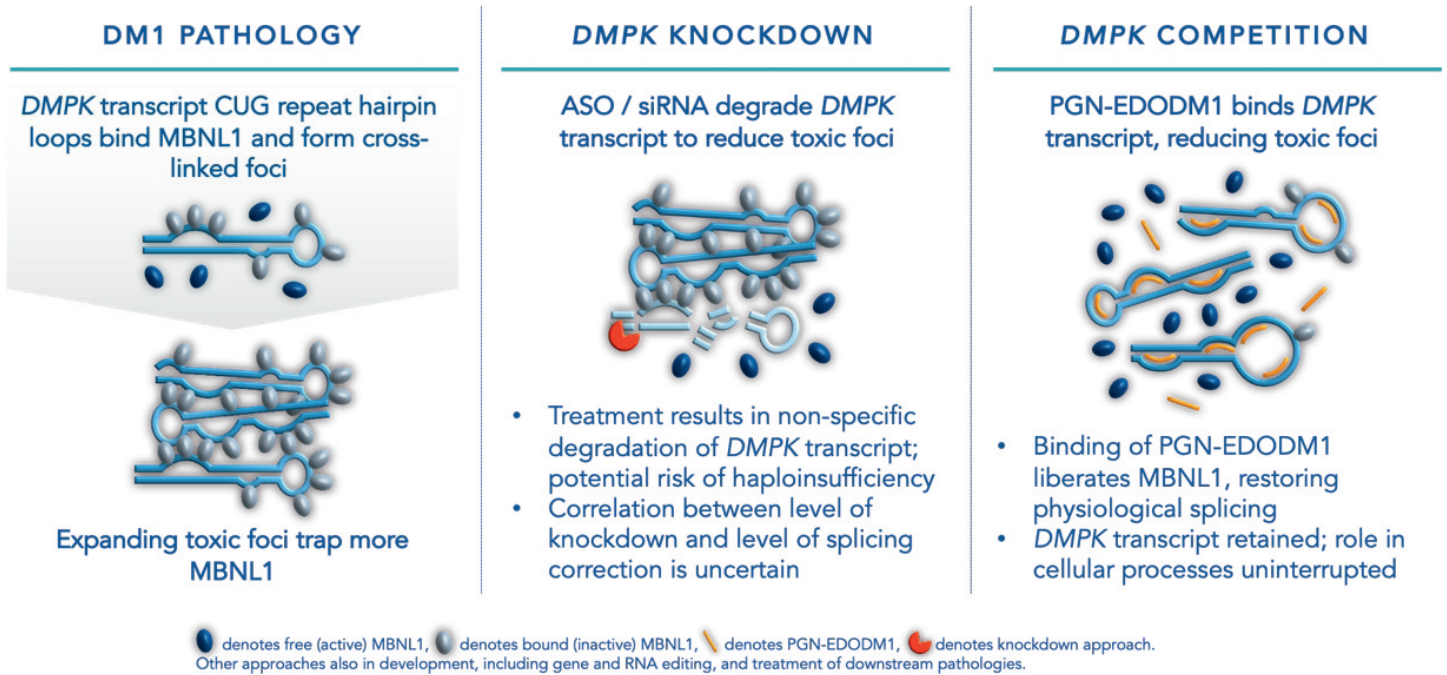
	EDO CONJUGATE	TFR1 FAB / MAB AOC
MECHANISM OF ACTION	Intended to target MBNL1 binding to <i>DMPK</i> transcripts, with no degradation of <i>DMPK</i> .	Degradation of <i>DMPK</i> risks confounding effects due to haploinsufficiency. Potential disconnect between <i>DMPK</i> knockdown and correction of mis-splicing.
	Not designed to require RISC or RNaseH proteins; potential for encouraging accessibility to toxic aggregated <i>DMPK</i> nuclear foci.	Requires RISC (siRNA oligonucleotide) or RNaseH (knockdown ASO) proteins.
DELIVERY TO MUSCLE	Considerably higher levels of oligonucleotide delivery observed in human muscle tissue in similar EDO candidate, PGN-EDO51, when compared to other exon 51 skipping approaches.	
	Efficient tissue penetration due to small size of EDO peptide relative to an antibody or antibody fragment.	Large size of delivery Fab / mAb reduces tissue penetration; Tfr1 receptor distribution may impact delivery.
DELIVERY TO THE NUCLEUS	EDO platform has shown successful delivery of therapeutic PMOs to the nucleus in preclinical studies, with robust exon skipping levels observed for PGN-EDO51.	
DELIVERY TO CNS	Delivery to CNS observed in NHPs following i.v. administration.	Affinity of Tfr1 Fab / mAb may prevent CNS delivery.
TOLERABILITY & IMMUNOGENICITY	Low risk of immunogenicity or complement activation.	Considerably higher protein load may lead to greater immunogenicity risk; mAb vectors risk complement activation.
MANUFACTURING SCALABILITY	Scalable, straightforward synthesis and characterization.	Increased complexity due to large size of Fab / mAb; may be reliant on cell-based processes.

We are additionally aware of other cell-penetrating peptide approaches currently in preclinical development for the treatment of DM1.

Our approach

Our product candidate for the treatment of DM1, PGN-EDODM1, consists of our lead EDO cell penetrating peptide conjugated to an ASO that binds to the CUG repeats 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, i.e. the sequestration of MBNL1 due to the high number of CUG repeats 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 *DMPK* transcript 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 deleterious outcomes.

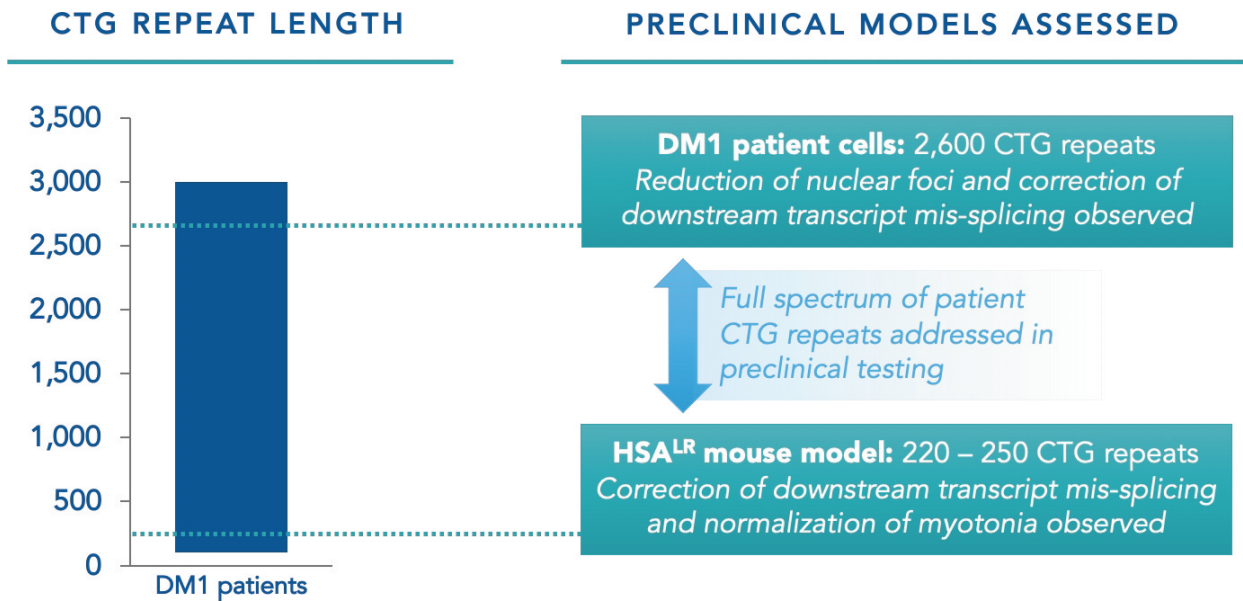


PGN-EDODM1 is designed to bind to the CUG repeats in *DMPK* RNA and liberate MBNL1 to restore physiological splicing, in contrast to modalities that target *DMPK* for knockdown.

Preclinical data

Activity data: Correction of molecular and functional DM1 phenotype

There is a considerable variation in the CTG repeat length present in DM1 patients, with patient population genotypes ranging from 50 repeats to almost 3,000. In order to demonstrate the potential ability of PGN-EDODM1 to address pathologies across this population, we have conducted our preclinical studies in models with a wide range of CTG repeat lengths that encompass those observed in the patient population. We have observed robust activity for PGN-EDODM1 across this spectrum from studies conducted in DM1 patient cells with 2,600 CTG repeats, to studies in the HSA^{L^R} mouse model, with 220 – 250 CTG repeats. We believe that this finding supports the clinical potential of PGN-EDODM1 in DM1 and highlights the relevance of this therapeutic approach to patients carrying long and short CTG repeat expansions.

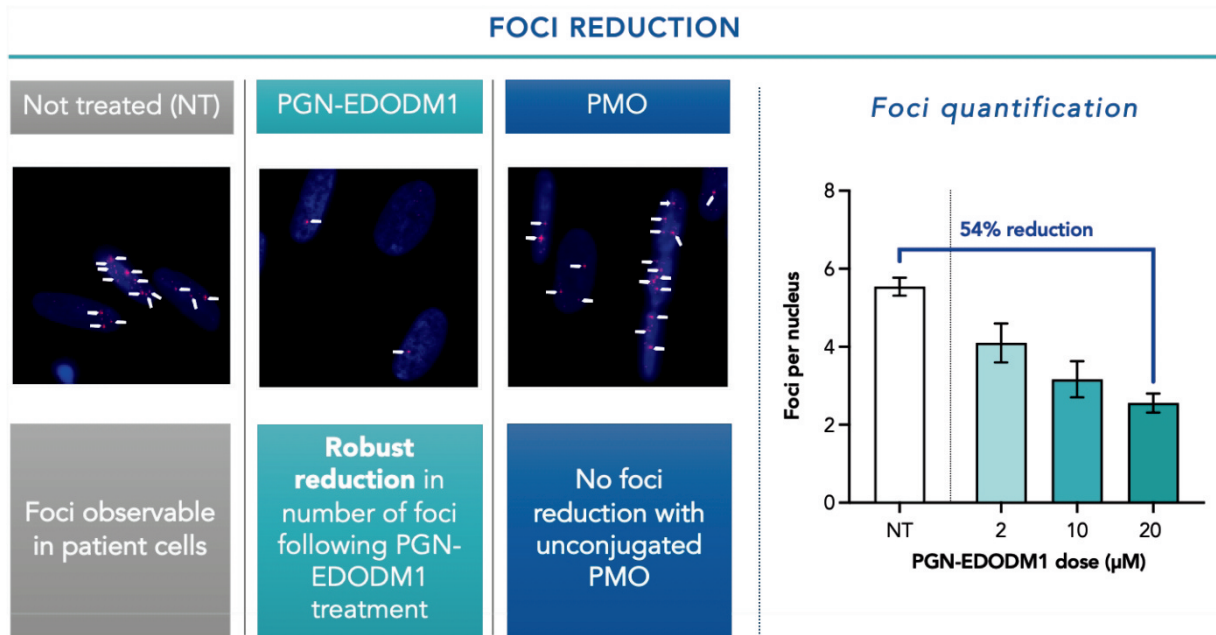


PGN-EDODM1 activity has been observed in preclinical models with a wide range of CTG repeat lengths.

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 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 ribonuclear 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 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

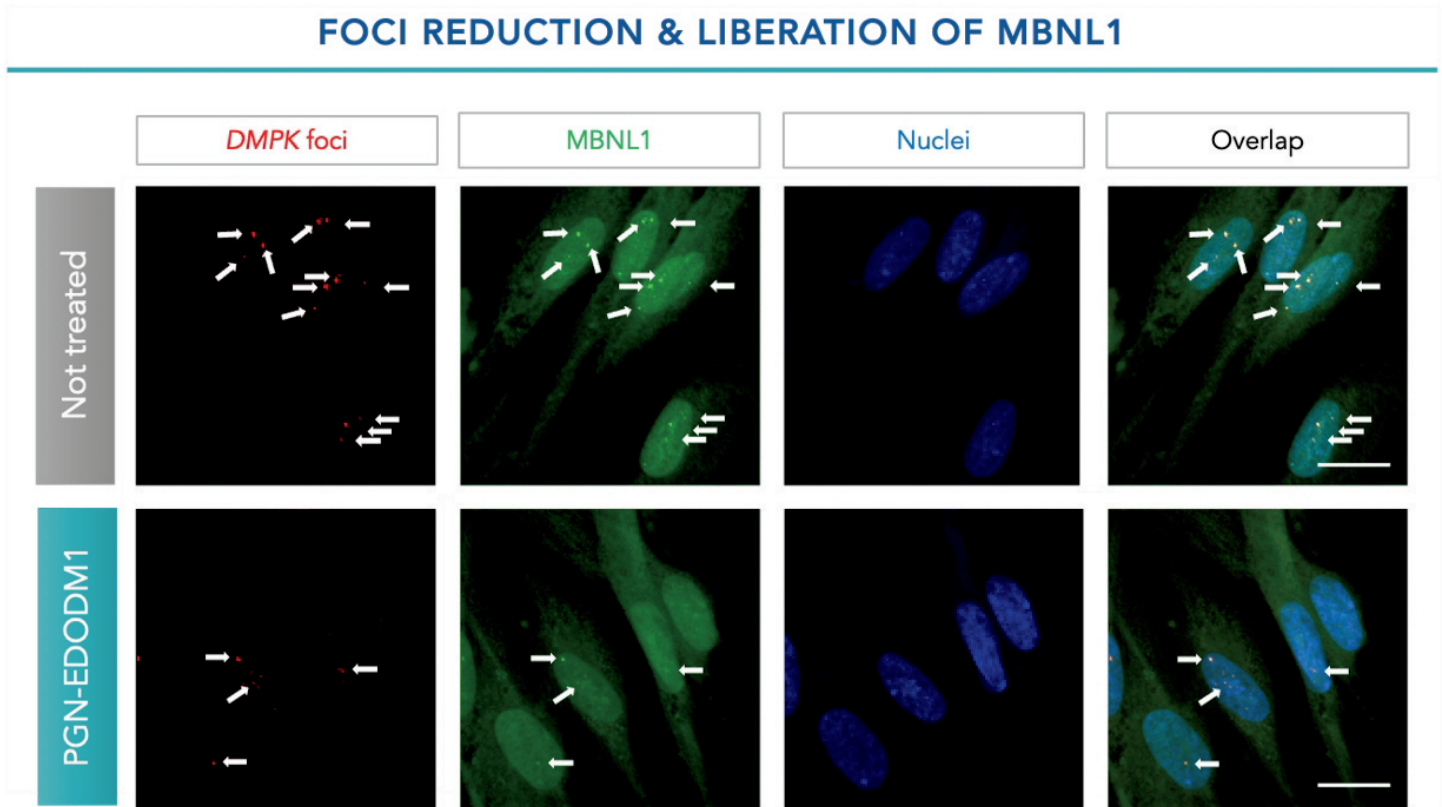
believe supports the potential utility of our EDO platform in driving the successful delivery of therapeutic agents to their nuclear site of action.



In a preclinical study conducted in DM1 patient cells, PGN-EDODM1 treatment supported the reduction of pathogenic nuclear foci in a dose-dependent fashion. Graph plotted as mean ± SD; n = 3-4 per group.

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 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

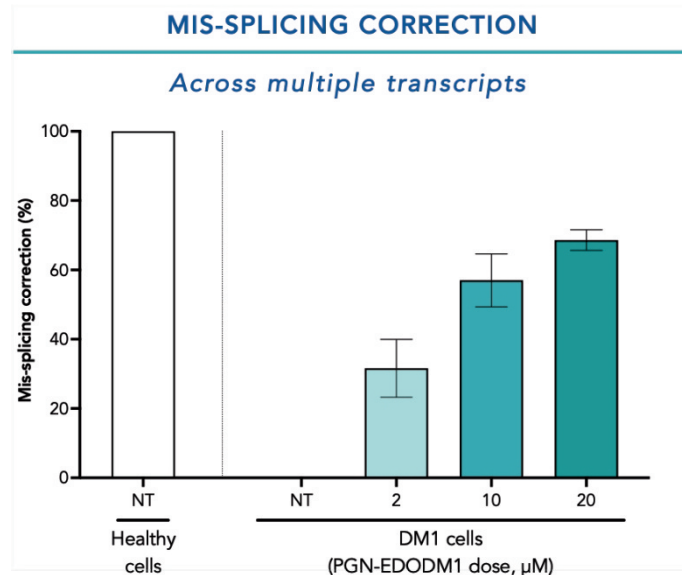
bind to the CUG repeat expansion present in the DPMK transcript, resulting in a reduction in the number of nuclear foci and the liberation of MBNL1.



PGN-EDODM1 treatment resulted in the liberation of MBNL1 from DPMK foci.

Treatment of DM1 patient cells with PGN-EDODM1 supported the robust correction of multiple downstream mis-spliced transcripts associated with key disease pathologies in a dose-dependent fashion. Utilizing RT-PCR and capillary electrophoresis analysis, an accurate, high resolution quantification methodology, we assessed the transcription profiles of MBNL1 and MBNL2, where pathogenic inclusion of exon 5 can result in further splicing defects; BIN1, where inclusion of exon 7 in DM1 patients can lead to altered excitation-contraction coupling and thus muscle weakness; LDB3, where exclusion of exon 11 may lead to dilated cardiomyopathy in DM1 patients; and SORBS1, where inclusion of exon 24 can result in altered insulin handling in the disease state. At the highest dose assessed, 20 μ M, PGN-EDODM1 was observed to effect robust mis-splicing correction, resulting in exon inclusion or exclusion rates of approximately 70% of healthy control levels in these transcripts. This observation supports our therapeutic hypothesis that treatment with PGN-EDODM1 may restore the altered global spliceopathy profiles seen in DM1 patients to that of a healthy individual, thus ameliorating the key pathologies that are the hallmark of this devastating disease. In contrast, treatment with the unconjugated PMO at a dose level of 20 μ M afforded very limited correction of downstream mis-splicing events,

and we believe this result further supports the criticality of our EDO platform in delivering therapeutic cargos to their nuclear site of action.



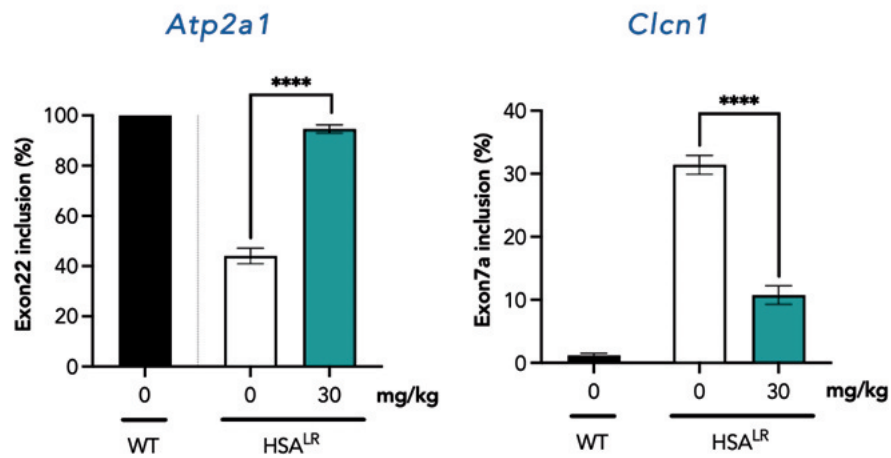
In an *in vitro* study, PGN-EDODM1 treatment resulted in correction of mis-splicing pathologies to around 70% of healthy control levels. Graph plotted as mean \pm SD; $n = 5$ per group.

Building on the success of these *in vitro* studies, we utilized the HSA^{LR} mouse model of DM1 to assess the activity of PGN-EDODM1. This well-validated transgenic mouse model contains between 220 and 250 CTG trinucleotide repeats in the inserted human skeletal actin 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 errant inclusions or exclusions of exons.

Sequestration of MBNL1 in the HSA^{LR} mouse model causes mis-splicing of multiple RNAs including *Cln1* and *Atp2a1*, both of which are involved in the regulation of muscle movement. This mis-splicing causes the mice to exhibit myotonia, effectively recapitulating the classic symptom of disease that is observed in DM1 patients. Mis-splicing of *Atp2a1* manifests as a lack of exon 22 inclusion in the *Atp2a1* mRNA when compared to wild-type splicing patterns, while mis-splicing of *Cln1* manifests as an increase in exon 7a inclusion in the *Cln1* mRNA when compared to wild-type splicing patterns. Following a single intravenous administration of PGN-EDODM1, we observed dose-dependent normalization of the splicing of these genes in the quadriceps and gastrocnemius

muscles two weeks after dosing. At a dose of 30 mg/kg, we achieved 91% correction of *Atp2a1* mis-splicing and 68% correction of *Clcn1* mis-splicing, highlighting the potential of our product candidate to address such downstream pathologies.

CORRECTION OF MIS-SPLICING



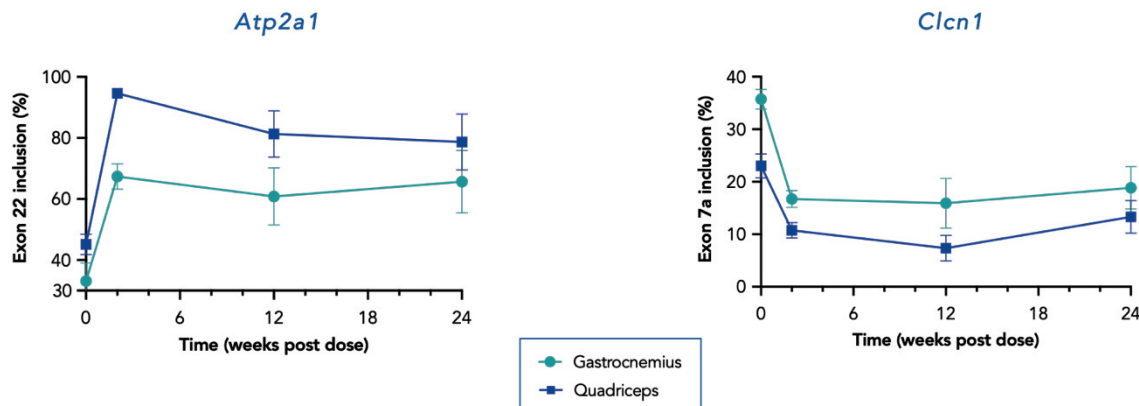
PGN-EDODM1 led to a dose-dependent normalization of the splicing of *Atp2a1* and *Clcn1* transcripts in preclinical study in quadriceps muscles in HSA^{LR} mice. Graph plotted as mean \pm SEM; $n = 8$ for PGN-EDODM1 group, $n = 16$ for HSA^{LR} saline control, $n = 8$ for WT saline control; **** = $p \leq 0.0001$.

Consistent with the reversal of mis-splicing events, treatment with a single dose of PGN-EDODM1 also led to a complete reversal of the myotonia phenotype in HSA^{LR} mice, with a dose of 30 mg/kg showing complete normalization two weeks after administration. In observational studies we noted quantitative amelioration of myotonia, where treated mice were able to ambulate normally following the inducement of this functional phenotype of disease by hindlimb pinching. In contrast, untreated HSA^{LR} mice were unable to efficiently use their hind legs and dragged them behind following the same myotonic inducement event.

PGN-EDODM1 led to a complete amelioration of myotonia in a preclinical study after a single administration. Graph plotted as min to max; $n = 8$ for PGN-EDODM1 group, $n = 16$ for HSA^{LR} saline control, $n = 8$ for WT saline control; *** = $p \leq 0.001$.

The pharmacologic effects of PGN-EDODM1 were observed to be highly durable. In a duration of effect study, again in the HSA^{LR} mouse model, amelioration of the pathogenic splicing patterns of the *Atp2a1* and *Clcn1* transcripts in the gastrocnemius and quadriceps persisted for at least 24 weeks following a single 30 mg/kg intravenous administration of PGN-EDODM1.

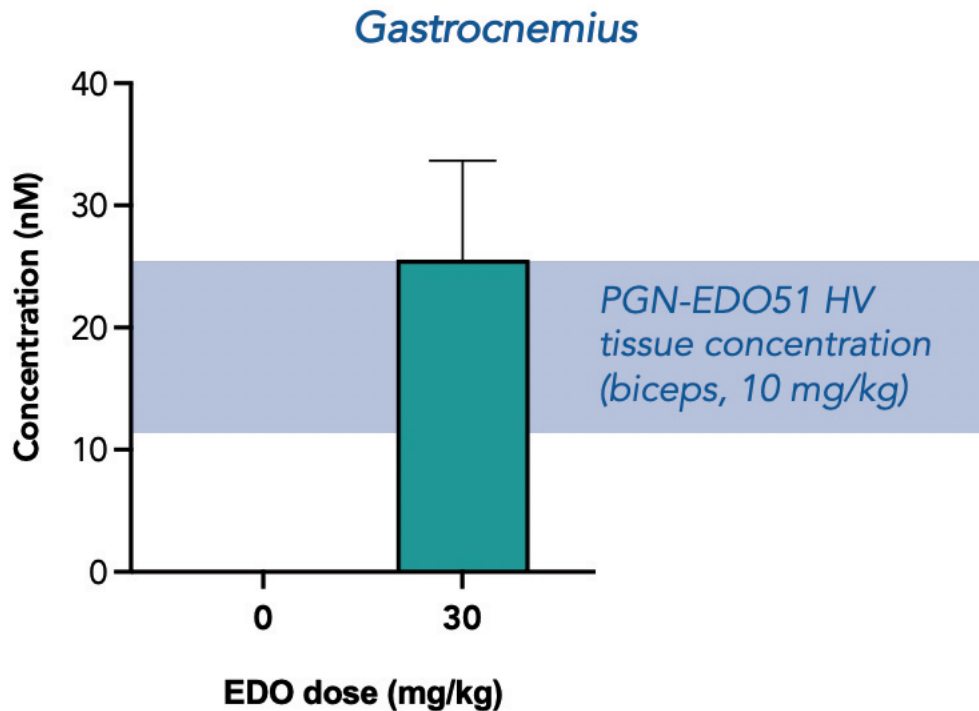
CORRECTION OF MIS-SPLICING



PGN-EDODM1 led to durable improvements in mRNA splicing through 24 weeks post-dose in the HSA^{LR} mouse model.
Graph plotted as mean ± SEM; n = 7 for 0 timepoint, 8 for 2- and 12-week timepoints; 5 for 24-week timepoint.

The clinical potential of PGN-EDODM1 is further supported by the readouts from our recently completed Phase 1 clinical trial of PGN-EDO51. In this trial, we observed tissue concentrations following a single dose of 10 mg/kg that were comparable to those observed in the HSA^{LR} mouse model following a single, pharmacologically active dose of 30 mg/kg. Based on this correlation, we believe that PGN-EDODM1 has the potential to achieve oligonucleotide tissue concentrations in DM1 patients that could lead to clinically meaningful outcomes, a factor which supports the further development of this product candidate.

HSA^{LR} TISSUE CONCENTRATION



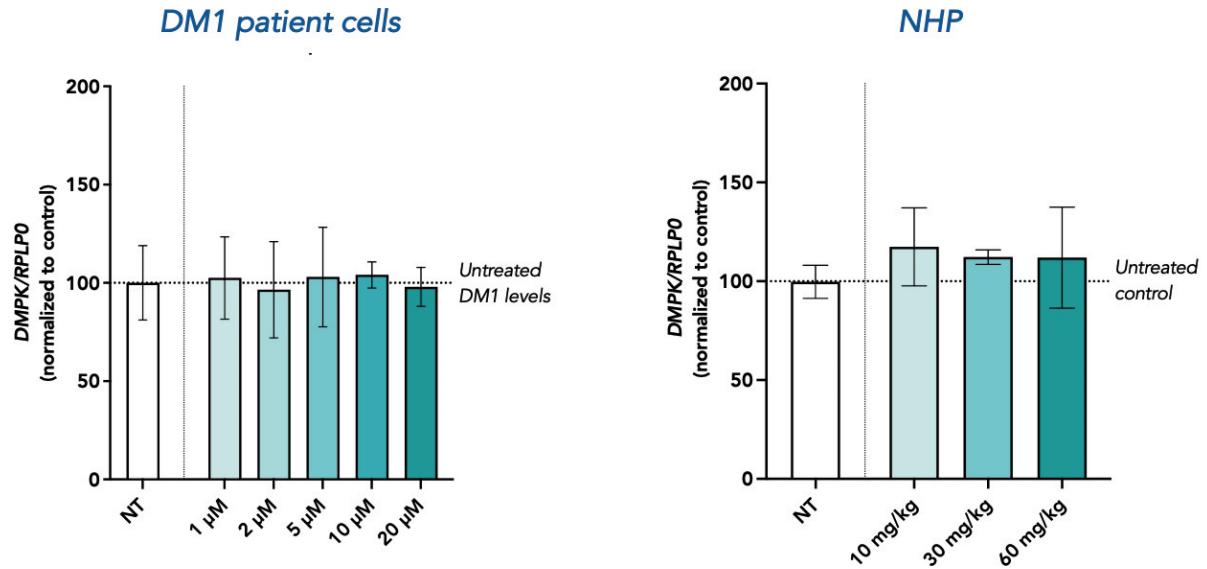
PGN-EDO51 tissue concentrations were comparable to those achieved for PGN-EDODM1 in HSA^{LR} mice. *Graph plotted as mean ± SEM; n = 8 for PGN-EDODM1 group, n = 8 for WT saline control; n = 6 for PGN-EDO51 data.*

Preclinical tolerability data: Well-tolerated through 90 mg/kg in NHP

We have completed a number of rigorous studies that support a well-tolerated safety profile for PGN-EDODM1. In an *in vitro* study, immortalized myoblasts from a DM1 patient with 2,600 CTG repeats were differentiated for 4 days to myotubes and treated for 24 hours with PGN-EDODM1 at a range of concentrations between 1 and 20 μ M. *DMPK* transcript levels were evaluated by qPCR and normalized to *Rplp0*. In NHPs, three doses of 10, 30 or 60 mg/kg of PGN-EDODM1 were administered every two weeks. One week following the final dose, *DMPK* transcript levels were evaluated by qPCR and normalized to *Rplp0*.

In both DM1 patient cells and in NHPs, mean *DMPK* transcript levels remained unchanged relative to an untreated control, and we believe that these results indicate that PGN-EDODM1, as designed, does not target *DMPK* transcripts for degradation. This unique mechanism of action is a potentially important safety benefit, as such an approach does not carry the risk of possible confounding effects due to the knockdown of *DMPK*.

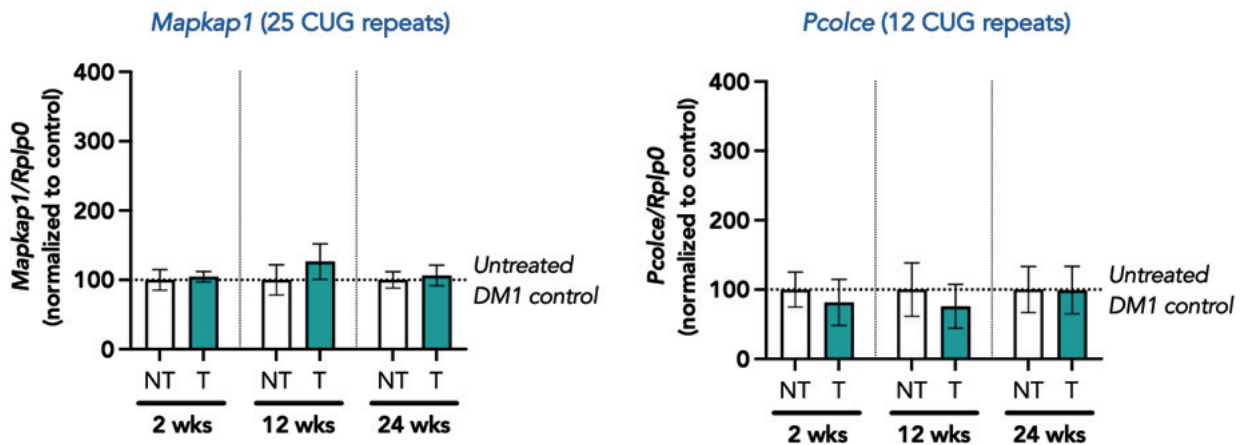
DMPK TRANSCRIPT LEVELS



No significant changes in mean *DMPK* transcript levels were observed in DM1 patient cells or in NHPs. Graphs plotted as mean \pm SEM; $n = 4$ for patient cell data, $n = 3-4$ for NHP data.

We have also assessed the potential for off-target effects in our preclinical work, and have not found any evidence of such findings in any of the studies conducted. In a single-dose study conducted in the HSA^{LR} mouse model, where PGN-EDODM1 was administered intravenously at a dose level of 30 mg/kg, we observed no short- or long-term impacts on the levels of other, non-*DMPK* transcripts containing more than 10 CUG repeats. Transcript levels were measured by qPCR, and were subsequently normalized to *Rplp0*. This study extended to a 24-week timepoint, and we believe that the data obtained suggests that there is limited risk of off-target complications for this approach in DM1 patients.

TRANSCRIPT LEVELS IN HSA^{LR} MOUSE (QUADS)

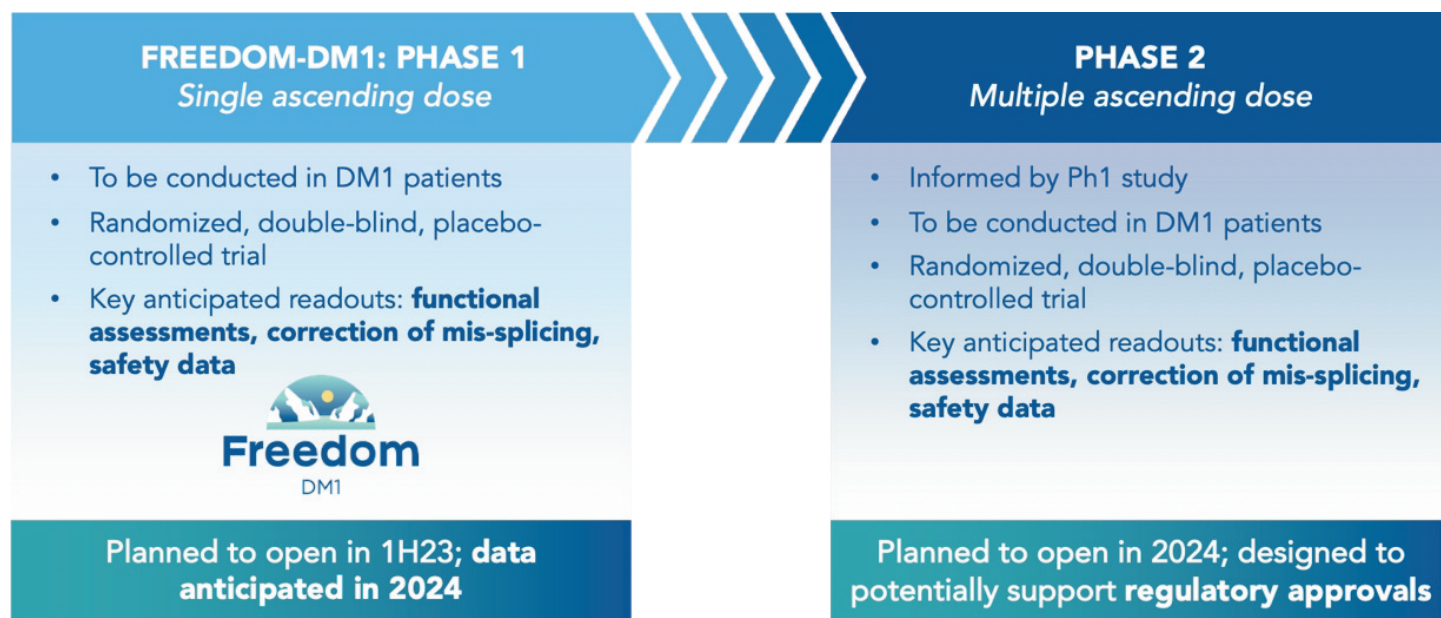


No significant impact was observed on the mean levels of other transcripts containing more than 10 CUG repeats. Graphs plotted as mean \pm SEM; $n=7$ for 0 timepoint, 8 for 2- and 12-week timepoints; 5 for 24-week timepoint; NT = not treated, T = treated.

Finally, in single-dose GLP toxicology studies conducted in NHP, PGN-EDODM1 was observed to be well-tolerated through dose levels of 90 mg/kg. There were no adverse effects on kidney, liver or cardiovascular function, and we believe that the totality of the data obtained from these preclinical and IND-enabling studies highlight a potentially favorable safety profile for PGN-EDODM1 and support the further progression of this product candidate to the clinic. We anticipate opening a single ascending dose clinical trial of PGN-EDODM1 in DM1 patients in the first half of 2023, with functional assessments, correction of mis-splicing and safety data expected in 2024.

Clinical development

Our clinical development program for PGN-EDODM1 has been designed to identify a clinically active dose while providing what we believe to be the shortest path to a potential approval. Our planned Phase 1 SAD study in DM1 patients, FREEDOM-DM1, is expected to be a randomized, double-blind placebo-controlled study that will provide critical information regarding the safety of escalating doses of PGN-EDODM1. Other anticipated readouts for this study include functional assessments and correction of mis-splicing data, which we expect to deliver in 2024. The data from our Phase 1 SAD trial is intended to support our planned Phase 2 randomized, double blind, placebo-controlled MAD study in DM1, which we anticipate opening in 2024. This study will incorporate functional assessments, correction of mis-splicing and safety readouts, and will be designed to support potential accelerated regulatory approvals.



We anticipate opening our first clinical trial in DM1 patients in the first half of 2023, with clinical readouts in 2024.

Additional DMD programs

Overview

We are developing additional EDO therapeutics for further DMD patient populations, including PGN-EDO53, for the 8% of DMD patients who are amenable to an exon 53-skipping approach, PGN-EDO45, for the 8% of DMD patients who are amenable to an exon 45-skipping approach, and PGN-EDO44, for the 6% of DMD patients who are amenable to an exon 44-skipping approach. These programs utilize the same EDO cell penetrating peptide as our exon 51-skipping product candidate, PGN-EDO51, which we believe will allow us to leverage our drug development experience in this indication to rapidly drive our exon 53, 45 and 44-skipping product candidates to the clinic. In a NHP study of PGN-EDO53, we observed single-dose exon skipping levels that were almost seven times higher than those observed for R₆G-PMO53, a relevant comparator peptide-PMO conjugate approach. For PGN-EDO45, high, dose-dependent levels of exon skipping were observed in wild-type human myoblasts, with our nominated candidate outperforming the R₆G-PMO45 comparator at every dose level assessed. Finally, our PGN-EDO44 nominated candidate also exhibited high, dose-dependent levels of exon skipping in wild-type human myoblasts.

Disease background and prevalence

DMD is a fatal X-linked recessive disorder that occurs in up to 1 in 3,500 live male births, with estimates suggesting that there are up to 15,000 DMD patients in the United States and approximately 25,000 in Europe and 5,000 in Japan. Afflicted individuals

carry a mutation in the dystrophin gene, and the resulting absence of this critical protein in muscle tissue leads to cell death, atrophy and progressive motoric weakness. As such, DMD sufferers experience a continual deterioration in their physical abilities from birth onwards, with most boys requiring the use of a wheelchair by their early teens. Cardiomyopathies and respiratory ailments become increasingly common as the disease takes hold, and most patients will die from these complications between the ages of 25 and 35. It is estimated that 8% of DMD patients have mutations that would be amenable to treatment with an exon 53-skipping approach, with exon 45- and 44-skipping approaches targeting a further 8% and 6% of the DMD patient population respectively.

Current approaches and limitations

Two unconjugated ASOs leveraging PMO chemistry have been approved for the treatment of individuals with DMD who are amenable to an exon 53-skipping approach – golodirsén, marketed as VYONDYS 53[®] by Sarepta and viltolarsén, marketed as VILTEPSO[®] by NS Pharma in the U.S. and Nippon Shinyaku in Japan. These drugs were approved in the United States through the accelerated approval regulatory pathway based on an increased expression of dystrophin, which is considered to be a surrogate endpoint for this indication. Both golodirsén and viltolarsén have yet to establish a clinical benefit for DMD patients through a confirmatory trial. For the exon 45 patient population, casimersén, marketed as AMONDYS 45[®] by Sarepta, has also been approved in the United States through the accelerated approval pathway, with a confirmatory trial yet to be completed for this unconjugated PMO. There are no approved therapeutics for the exon 44 patient population.

Our approach

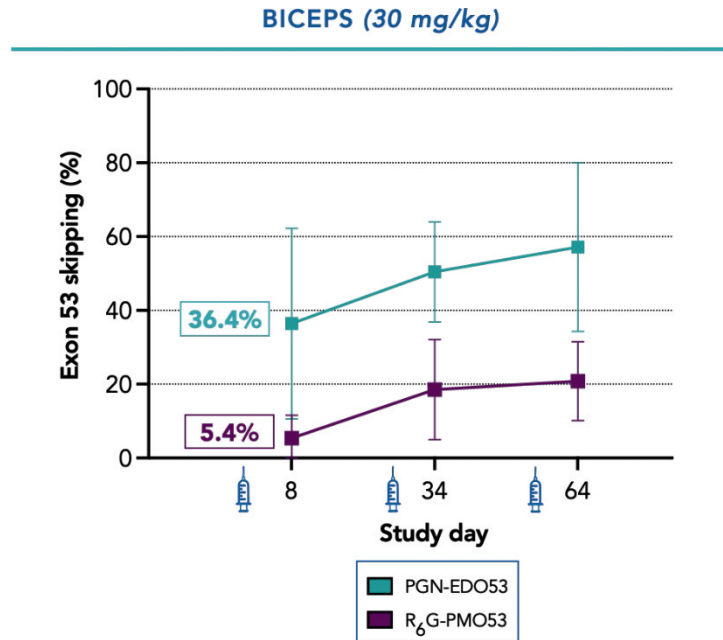
We are developing PGN-EDO53, a peptide-conjugated ASO designed to skip exon 53 of the dystrophin transcript in DMD patients who are amenable to such a therapeutic approach. We have employed the same EDO peptide in PGN-EDO53 as is utilized in PGN-EDO51, our exon 51-skipping product candidate – a factor that allows us to rapidly drive our exon 53-skipping product candidate forward by leveraging our drug development experience with this peptide and in this indication. Similarly, PGN-EDO45 and PGN-EDO44, our peptide-conjugated ASOs designed to skip exons 45 and 44 of the DMD transcript respectively, also leverage the capabilities of our lead EDO peptide.

Preclinical development

PGN-EDO53

We have completed a preclinical *in vitro* screen of a number of candidate ASO sequences utilizing the established PMO chemistry. We synthesized a number of exon 53-skipping PMOs conjugated to our lead EDO peptide and assessed the activity of these in human-derived myoblasts carrying mutations that are amenable to treatment with an exon 53-skipping therapeutic approach. Based on the data obtained from this *in vitro* screen, we have subsequently assessed several development candidates in a repeat-dose NHP study, where these PPMOs were assessed alongside a relevant comparator, R₆G-PMO53. Three doses of each PPMO were administered intravenously over 60 minutes every four weeks, with biopsies of the biceps collected 5 to 7 days after the first and second administrations, and terminal samples collected 7 days after the final dose. Exon 53 skipping was assessed by RT-PCR.

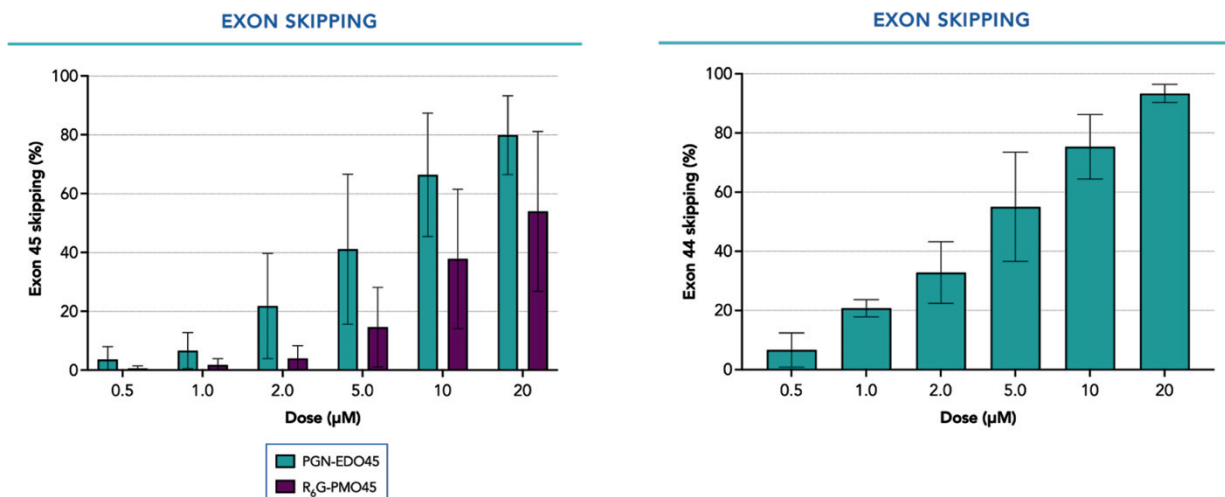
Notably, the single-dose exon skipping levels of 36.4% obtained for the selected PGN-EDO53 candidate were almost seven times higher than those observed for the R₆G-PMO53 comparator at 5.4%. Furthermore, exon 53 skipped transcripts accumulated with repeat dosing of PGN-EDO53 – following the third and final dose of PGN-EDO53, mean exon skipping levels were observed to be 57.2%, a level that was nearly three-times higher than the mean exon skipping levels of 20.8% that were observed for the R₆G-PMO53 comparator. We believe that this accumulation in skipped transcript is indicative of the potential of the EDO platform to drive clinically meaningful levels of exon skipping, and ultimately dystrophin production, in DMD patients.



Treatment with PGN-EDO53 afforded single-dose exon skipping levels almost seven times higher than for a comparator PPMO. Graphs plotted as mean \pm SD; n = 3 per group; study was not powered for statistical significance.

PGN-EDO45 and PGN-EDO44

We have completed an *in vitro* screen for our PGN-EDO45 and PGN-EDO44 programs in order to nominate potential candidates for further development. In these studies, wild-type human myoblasts were treated for 48 hours with the PPMO compounds, and exon 45 or exon 44 skipping levels were assessed by RT-PCR. For PGN-EDO45, we observed high, dose-dependent levels of exon 45 skipping, with this product candidate outperforming a R₆G-PMO45 comparator compound at each dose level assessed. At the highest dose, PGN-EDO45 demonstrated mean exon 45 skipping levels of 79.9%, while R₆G-PMO45 demonstrated only 54.0%. For PGN-EDO44, high, dose-dependent levels of exon 44 skipping were also observed, with a readout of 93.4% obtained at the highest dose. No comparator compound was included in this study.



High levels of exon skipping were observed for PGN-EDO45 and PGN-EDO44 in wild-type human myoblasts. *Graphs plotted as mean \pm SD; n = 4 for PGN-EDO45 and R₆G-PMO (n = 3 for R₆G-PMO at two top dose levels), n = 3 for PGN-EDO44.*

We believe that these data highlight the ability of our EDO technology to enable the rapid development of our pipeline programs, and support the modularity of this approach.

Expanding the Application and Scope of Our EDO Platform

New indications with PMO therapeutics

We intend to apply our deep understanding of our EDO platform and PMO therapeutics to the development of additional product candidates in other indications. We believe that the ability of our EDO peptides to deliver exon skipping therapeutics to muscle cells, including cardiac muscle cells, as well as to the CNS, is largely independent of the exact sequence of the PMO. As such, by leveraging the preclinical data we have previously obtained and the “plug-and-play” nature of our EDO platform, we believe that we are well-positioned to develop additional product candidates that have the potential to drive clinically relevant therapeutic outcomes in other neuromuscular indications as well as in neurologic indications. We have observed the potential of this approach with our PGN-EDO53 program, where we progressed from concept through to NHP study initiation in less than a year.

New cargos

We believe that our EDO technology has the potential to facilitate the delivery of multiple oligonucleotide therapeutics. To date, our efforts have primarily focused on the delivery of PMOs, but we are now actively pursuing 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. We will leverage our deep expertise in this field to design new peptides that target specific tissue types, and will seek to further optimize the tissue and cellular delivery of our EDO platform.

Manufacturing

We do not own or operate manufacturing facilities, and currently rely on third-party contract manufacturing organizations, or CMOs, and suppliers for the cell-penetrating peptide, 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 CMOs 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 CMOs are able to assemble either the peptide intermediate, the linker, and/or the oligonucleotide as well as the final API.

There are extensive regulations that govern the manufacturing of biopharmaceutical products, and the third-party manufacturing organizations we work with are required to adhere to these. Our CMOs are required to manufacture our product candidates under current Good Manufacturing Practice, or 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. Individuals with DMD also use prednisone or prednisolone off-label. In addition, there are four FDA-approved exon skipping drugs: EXONDYS 51 (Eteplirsen), VYONDYS 53 (Golodirsen) and AMONDYS 45 (Casimersen), which are naked PMOs approved for the treatment of DMD patients amenable to exon 51, exon 53 and exon 45 skipping, respectively, and are 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. Companies focused on developing treatments for DMD that target dystrophin, as our DMD program does, include PTC with ataluren, a small molecule targeting nonsense mutations in a Phase 3 clinical trial, Sarepta with SRP-5051, a peptide-linked PMO currently being evaluated in a Phase 2b clinical trial for patients amenable to exon 51 skipping, Daiichi Sankyo Company, Limited with DS-5141b, an exon skipping approach for Exon 45 currently in clinical development, Dyne, with DYNE-251, an antibody-conjugated PMO that targets exon 51 skipping in a Phase 1/2 clinical trial, BioMarin Pharmaceutical Inc. with BMN-351, a phosphorothioate oligonucleotide that targets exon 51 skipping currently in preclinical development, Wave Life Sciences Ltd. with WVE-N531, a stereopure oligonucleotide in clinical development for patients amenable to exon 53 skipping, Nippon Shinyaku with NS-089/NCNP-02, an oligonucleotide that targets exon 44 skipping that is currently in clinical development, Avidity Biosciences, Inc., or Avidity, which is in Phase 1/2 clinical development with AOC 1044, an antibody oligonucleotide conjugate that targets Exon 44 skipping, and Entrada Therapeutics, Inc., which is in preclinical development with ENTR-601-44, a peptide-oligonucleotide conjugate that targets Exon 44 skipping and with a clinical hold placed on its investigational new drug application (IND) by the FDA prior to dosing of the first healthy volunteer.

In addition, several companies are developing gene therapies to treat DMD, including Pfizer Inc. (PF-06939926), currently being evaluated in a Phase 3 clinical trial, Sarepta (SRP-9001 and Galgt2 gene therapy program), with the former currently being evaluated in a Phase 3 clinical trial and with a BLA under review by the FDA for accelerated approval, Solid Biosciences Inc. (SGT-003), currently in preclinical development, and REGENXBIO Inc (RGX-202), currently in clinical development. Gene editing treatments that are in preclinical development are also being pursued by Vertex Pharmaceuticals Incorporated, or Vertex, Sarepta and Eli Lilly and Company. We are also aware of several companies targeting non-dystrophin mechanisms for the treatment of DMD, including Edgewise Therapeutics, Inc., with EDG-5506, a muscle stabilizer that is currently in clinical development.

There are currently no approved therapies to treat the underlying cause of DM1. Product candidates currently in development to treat DM1 include: tideglusib, a GSK3- β inhibitor in late-stage clinical development by AMO Pharma Ltd. for the congenital phenotype of DM1; AOC 1001, an antibody linked siRNA in Phase 1/2 clinical development by Avidity Biosciences, Inc.; DYNE-101, an antibody conjugated antisense oligonucleotide in clinical development by Dyne; a microRNA small molecule approach by Arthex Biotech S.L. in preclinical development; gene editing treatments in preclinical development by Vertex; an artificial site-specific RNA endonuclease gene therapy being developed by Enzerna Biosciences Inc.; an RNA-targeting gene therapy in preclinical development by Locana, Inc.; an approach by Design Therapeutics, Inc. to prevent formation of CUG hairpins; an approach utilizing the interaction of small molecules with RNA in preclinical development by Expansion Therapeutics, Inc.; a peptide conjugated PMO in preclinical development by Entrada Therapeutics and Vertex; and therapeutics based on biomolecular condensate biology in preclinical development by Dewpoint Therapeutics, Inc., 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 Pharmaceuticals, Inc., Aro Biotherapeutics Co, Arrowhead Pharmaceuticals, Inc., Avidity, Dicerna Pharmaceuticals, Inc. (acquired by Novo Nordisk), Dyne, Entrada Therapeutics, Inc., Ionis Pharmaceuticals, Inc., NeuBase Therapeutics, Inc., PYC Therapeutics Limited 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 United States 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 salesforce, 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 United States that we may identify, where appropriate, we may utilize strategic partners, distributors or contract sales forces to expand the commercial availability of our product candidates.

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 Medical Research Council as Part of United Kingdom Research and Innovation, or 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 a of 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 milestones in an aggregate amount of £100,000 for each OUI/MRC Licensed Product and specified patent procurement milestones in an aggregate amount of £10,000.

Upon completion of the Company's initial public offering, or IPO in May 2022, the Company 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 after November 23, 2023 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 United States that also claim technology or therapeutics to which we have rights, we may have to participate in interference proceedings in the United States 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. 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 United States, the patent term is 20 years from the earliest filing date of a non-provisional patent application. In the United States, 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, 2022, we owned two pending U.S. patent applications and two pending PCT international applications, and exclusively licensed one issued patent (a European patent validated in France, Germany, Italy, Spain, and Great Britain) and 58 patent applications under our PepGen Inc's license with Oxford University Innovation Limited, or OUI, and Medical Research Council of United Kingdom Research and Innovation, or MRC. For more information regarding our license agreement with OUI and MRC, or 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 include:

- With respect to PGN-EDO51, we own one pending U.S. patent application and one pending PCT international application that cover methods of use and exclusively licensed 32 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 United States, as well as two PCT international applications. Any patents issuing from the patent applications would have expiration dates ranging from 2039 to 2043, without accounting for any available patent term adjustments or extensions.
- With respect to PGN-EDODM1, we owned one pending PCT international patent application that covers methods of use and exclusively licensed 45 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 United States. 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 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 United States. Any patents issuing from these patent applications would expire in 2039, without accounting for any available patent term adjustments or extensions.

- With respect to our EDO platform, we own one pending U.S. patent application and exclusively licensed one issued European patent and 41 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 United States. 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 United States, 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 United States generally involves the following:

- Completion of preclinical laboratory tests, animal studies and formulation studies in compliance with the FDA's good laboratory practice, or GLP, regulations;
- Submission to the FDA of an investigational new drug application, or 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 Practices, 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 current good manufacturing practice, or 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 good laboratory practice regulations for safety/toxicology studies.

Prior to beginning the first clinical trial with a product candidate in the United States, we must submit an IND to the FDA. An IND 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 data safety monitoring board, which provides authorization for whether or not a study may move forward at designated check points based on access to certain data from the study and may halt the clinical trial if it determines that there is an unacceptable safety risk for subjects or other grounds, such as no demonstration of efficacy.

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 serious adverse events 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 United States, or (ii) more than 200,000 individuals in the United States and for which there is no reasonable expectation that the cost of developing and making the product available in the United States for this type of disease or condition will be recovered from sales of the product. 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 United States 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 United States to the first applicant to gain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not accept for review an 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 United States. Pediatric exclusivity, if granted, adds six months to existing regulatory exclusivity periods or listed patents. 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. 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 United States. 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. 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 United States.

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.

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 United States, in March 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.

Since its enactment, there have also been numerous judicial, administrative, executive, and legislative challenges to certain aspects of the ACA. 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 to 2030, unless additional Congressional action is taken.

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 issued by the former Trump administration designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products. It is also possible that additional governmental action is taken in response to the ongoing COVID-19 pandemic. Individual states in the United States 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 United States, numerous federal and state laws and regulations, including data breach notification laws, health information privacy and security laws and consumer protection laws and regulations 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 EU does not consider to have in place adequate data protection legislation, including the United States. 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 United

Kingdom, 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.

Brexit and the Regulatory Framework in the United Kingdom

The UK formally left the EU on January 31, 2020, and the EU and the UK have concluded a trade and cooperation agreement, or TCA, which was provisionally applicable since January 1, 2021 and has been formally applicable since May 1, 2021. The TCA includes specific provisions concerning pharmaceuticals, which include the mutual recognition of cGMP, inspections of manufacturing facilities for medicinal products and cGMP documents issued, but does not foresee wholesale mutual recognition of United Kingdom and EU pharmaceutical regulations. At present, EU laws which have been transposed into UK law through secondary legislation continue to be applicable as “retained EU law”. However, new legislation such as the EU Clinical Trials Regulation or in relation to orphan medicinal products will not be applicable. The UK 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 of January 1, 2021, the Medicines and Healthcare products Regulatory Agency, or MHRA, is the UK’s standalone medicines and medical devices regulator. As a result of the Northern Ireland protocol, different rules will apply in Northern Ireland than in England, Wales, and Scotland (together, Great Britain, or GB); broadly, Northern Ireland will continue to follow the EU regulatory regime, but its national competent authority will remain the MHRA.

The MHRA has introduced changes to national licensing procedures, including procedures to prioritize access to new medicines that will benefit patients, including a 150-day assessment and a rolling review procedure. All existing EU marketing authorizations for centrally authorized products were automatically converted or grandfathered into UK marketing authorizations, effective in Great Britain (only), free of charge on January 1, 2021, unless the marketing authorization holder chose to opt-out. In order to use the centralized procedure to obtain a marketing authorization that will be valid throughout the EEA, companies must be established in the EEA. Therefore, since Brexit, companies established in the UK can no longer use the centralized procedure and instead an EEA entity must hold any centralized marketing authorizations. In order to obtain a UK marketing authorization to commercialize products in the UK, an applicant must be established in the UK or EEA and must follow one of the UK national authorization procedures. For a period of three years from January 1, 2021, the MHRA may rely on a decision taken by the European Commission on the approval of a new (centralized procedure) marketing authorization when determining an application for a GB authorization. A separate application for the GB authorization is, however, still required. On January 24, 2023, the MHRA announced that a new international recognition framework will be put in place from January 1, 2024, which will have regard to decisions on the approval of marketing authorizations made by the European Medicines Agency and certain other regulators when determining an application for a GB 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 GB authorization.

There is no longer pre-marketing authorization orphan designation in GB. 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 GB, 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 GB.

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

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

Employees and Human Capital Resources

As of December 31, 2022, we had 45 full-time employees, of which 20 have Ph.D. degrees, and several part-time employees employed on a co-op or internship basis. Within our workforce, 37 employees are engaged in research and development and eight are engaged in business development, finance, legal, 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 2022, we primarily operated out of approximately 800 square feet of office space located at 245 Main Street, Cambridge, Massachusetts 02142 and 6,500 square feet of laboratory space at the University of Massachusetts, Mount Ida Campus in Newton, Massachusetts at the School of Applied Sciences Building. The lease for our office space in Cambridge was on a month-to-month basis with a 30-day written notice of cancellation. The lease for our lab space had an original term of February 1, 2022 through January 2023, which we extended to March 2023. We also lease 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 current term of the lease is 110 months, expiring in March 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.

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 Securities and Exchange Commission, or 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 \$69.1 million and \$27.3 million for the year ended December 31, 2022 and December 31, 2021, respectively. As of December 31, 2022, we had an accumulated deficit of \$102.9 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 initial public offering. 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 one product candidate 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:

- complete preclinical and clinical activities for our programs in DMD and DM1 and advance them into and through clinical development;
- 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;
- 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;
- establish manufacturing sources for our product candidates and secure supply chain capacity to provide sufficient quantities for preclinical and clinical development and commercial supply;
- 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 recently completed our Phase 1 clinical trial for PGN-EDO51, we expect that it will be many years, if ever, before we have a product candidate ready for commercialization. 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 authorization 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. We recently completed a Phase 1 clinical trial for our first product candidate, PGN-EDO51. 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. 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, 2022, we had cash and cash equivalents of \$181.8 million. In July 2021, we raised aggregate gross proceeds of \$21.0 million from the final milestone closing of our Series A-2 convertible preferred stock and, additionally, in July 2021, we raised aggregate gross proceeds of \$112.5 million from the private placement of our Series B convertible preferred stock. In addition, in May 2022, we raised aggregate gross proceeds of \$122.9 million from our IPO.

Based on our current operating plans, we believe that our cash and cash equivalents will enable us to fund our operating expenses and capital expenditure requirements into early 2025. 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;
- the scope, costs, timing and outcome of regulatory review of our product candidates;
- 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 is a time-consuming, expensive and uncertain process that takes 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, recently completed a Phase 1 clinical trial and 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 transition at some point from a company with a research focus to a company capable of conducting development activities 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 very early in our development efforts. We have only completed a Phase 1 clinical trial of one 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.

We are very 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 are in the early stages of developing five product candidates—PGN-EDO51, PGN-EDODM1, PGN-EDO53, PGN-EDO45 and PGN-EDO44. We have completed the Phase 1 clinical trial for our first product candidate, PGN-EDO51; however, we 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 United States 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 first clinical trials may be delayed. Even after we receive and incorporate guidance from these regulatory authorities, the FDA or other regulatory authorities could disagree that we have satisfied their requirements to commence any clinical trial 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 the Europe.

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 authorization 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 GCPs, GLPs, 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 treat a variety of degenerative neuromuscular diseases and to be disease-modifying.

Our lead product candidate is 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 and in future clinical studies. In addition, our potential product candidates may not show promising signals of therapeutic effect in such experiments, 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.

We have advanced our lead product candidate, PGN-EDO51, into the clinic, and have recently completed a Phase 1 trial in HVs. However, the positive results we have observed in the completed Phase 1 trial may not be repeated in future clinical trials and regulatory authorities may disagree with the interpretation of data from this trial.

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;
- 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 authorization 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.

Clinical trials may fail to demonstrate that our product candidates are safe for humans and effective for indicated uses, and earlier results 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. Although we have completed a Phase 1 study of our lead product candidate, PGN-EDO51, 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, EMA or comparable foreign regulatory authorities will accept our proposed clinical programs or whether the outcome of our preclinical testing and studies will ultimately support the further development of our other product candidates. 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 preclinical 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, European Medicines Agency, or EMA, or comparable foreign regulatory authorities allowing clinical trials to begin.

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 United States, 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; or
- lack of adequate funding to continue the clinical trial.

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 data safety monitoring board 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 ongoing COVID-19 pandemic 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 modified risk evaluation and mitigation strategy, or 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 product candidates are rare genetic diseases 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 to try alternative therapies.

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 clinical trial in Canada for our lead product candidate, but 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 and our completed Phase 1 clinical trial. 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. In addition, initial success in clinical trials 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 ongoing COVID-19 pandemic.

Our inability to enroll a sufficient number of patients for clinical trials 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. 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.

While we have only completed dosing up to 15 mg/kg in a Phase 1 clinical trial of PGN-EDO51, in which PGN-EDO51 was generally well-tolerated at clinically active doses, 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 dose-limiting toxicity. 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.

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, results of our planned clinical trials 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. 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 will face an inherent risk of clinical trial and product liability exposure related to the testing of product candidates that 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 one product candidate 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 of our clinical trials for our product candidates outside of the United States. 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 United States. Although the FDA may accept data from clinical trials conducted outside the United States, 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 United States, 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 United States 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 United States. 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 United States 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 contract development manufacturing organizations, or 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 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 current Good Manufacturing Practices, or 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 who have the capability to both, on the one hand, manufacture oligonucleotides and peptides, and, on the other hand, conjugate them, both of which processes are critical to the development and production of our product candidates. We are aware that one or more competitors have engaged 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.

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 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 a 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 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, 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 preclinical studies or clinical trials of product candidates;
- delays 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 may compete with third parties for access to manufacturing facilities. 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.

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 IT 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 the ongoing COVID-19 pandemic, 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 candidate is 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 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 our first product candidate, 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 for our lead product candidate, PGN-EDO51, only. 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, PGN-EDO53, PGN-EDO45, PGN-EDO44 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 plan to open a Phase 2 multiple ascending dose clinical trial in DMD patients in the first half of 2023. In addition, we plan to open a Phase 1 trial of PGN-EDODM1 in DM1 patients in the first half of 2023 and commence our single ascending dose clinical trial, subject to receiving authorization to proceed under an IND. Based on the observed high levels of oligonucleotide delivery and exon skipping in muscle in our Phase 1 trial of PGN-EDO51, we believe that these results could signal the potential for the accumulation of exon 51 skipped transcript and dystrophin protein in muscle tissue with repeated doses of PGN-EDO51 in people living with DMD. However, our belief based on the Phase 1 clinical trial with HVs may be erroneous. There can be no assurance that our expectations of higher exon skipping and dystrophin production will be reflected in clinical evaluation of PGN-EDO51 with respect to people living with DMD.

Although we completed a Phase 1 clinical trial for our lead product candidate, we have not conducted any additional clinical trials, have limited experience as a company in preparing, submitting and prosecuting regulatory filings, and have submitted a CTA, which was subsequently authorized in Canada, for our lead product candidate only. We have not previously submitted an IND or an NDA for any product candidate. 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, PGN-EDO53, PGN-EDO45, PGN-EDO44 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. The FDA has provided feedback on both of our clinical programs, and we plan to incorporate their feedback into our clinical trials to support the potential for accelerated approval. We may be unable to successfully and efficiently execute and complete necessary clinical trials in a way that leads to regulatory submission and approval of any of our product candidates. 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 United States, 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 United States 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. 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 United States;
- 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 post-marketing confirmatory trial of PGN-EDO51, if it is approved under the accelerated approval regulations requiring applicants to demonstrate clinical benefit in post-approval studies. 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 United States 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 European Union 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 United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the United States, 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 United States 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 United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. We may not be able to file for marketing approvals and may not receive necessary approvals to commercialize our medicines in any jurisdiction, which would materially impair our ability to generate revenue.

Additionally, we could face heightened risks with respect to seeking marketing approval in the United Kingdom as a result of the recent withdrawal of the United Kingdom from the European Union, commonly referred to as Brexit. Pursuant to the formal withdrawal arrangements agreed between the United Kingdom and the European Union, the United Kingdom withdrew from the European Union, effective December 31, 2020. On December 24, 2020, the United Kingdom and the European Union entered into a Trade and Cooperation Agreement. The agreement sets out certain procedures for approval and recognition of medical products in each jurisdiction.

Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of the Trade and Cooperation Agreement or otherwise, would prevent us from commercializing any product candidates in the United Kingdom and/or the European Union 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 United Kingdom and/or the European Union 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 irreversible morbidity or mortality, or 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. For example, if we receive positive results from our Phase 2 trials 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. However, our anticipated Phase 2a clinical trial may fail to produce such data, and we may be unable to pursue the accelerated approval pathway as planned. 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 European Medicines Agency's Committee for Medicinal Products for Human Use 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 United States.

We may seek fast track designation for some of our 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. Even if we do receive 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 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.

We may seek orphan drug designation for some of our 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 United States, or a patient population greater than 200,000 in the United States where there is no reasonable expectation that the cost of developing the drug will be recovered from sales

in the United States. Orphan drug designation must be requested before submitting an NDA. A similar regulatory scheme governs orphan products in the European Union.

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 that 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.

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 manufacturer 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.

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.

Separately, in response to the ongoing COVID-19 pandemic, since March 2020, when foreign and domestic inspections of facilities were largely placed on hold, the FDA has been working to resume pre-pandemic levels of inspection activities, including routine surveillance, bioresearch monitoring and pre-approval inspections on a prioritized basis. Should the FDA determine that an inspection is necessary for approval and an inspection cannot be completed during the review cycle due to restrictions on travel, and the FDA does not determine a remote interactive evaluation to be adequate, the agency has stated that it generally intends to issue, depending on the circumstances, a complete response letter or defer action on the application until an inspection can be completed. 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. Regulatory authorities outside the United States may adopt similar restrictions or other policy measures in response to the ongoing COVID-19 pandemic. If a prolonged government shutdown occurs, or if global health concerns continue to prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews or other regulatory activities, it could significantly impact the ability of the FDA or other regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

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 the following:

- the federal healthcare anti-kickback statute, which prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration (including any kickback, bribe or rebate), directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, lease, order, arrangement or recommendation of, any good, facility, item or service, for which payment may be made under federal and state healthcare programs such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the federal Anti-Kickback Statute or specific intent to violate it to have committed a violation. Violations are subject to civil and criminal fines and penalties for each violation, plus up to three times the remuneration involved, imprisonment, and exclusion from government healthcare programs;
- the federal civil and criminal false claims laws, including the federal False Claims Act, and civil monetary penalty laws which can be enforced through civil whistleblower or qui tam actions, impose civil and criminal penalties against individuals or entities for knowingly presenting or causing to be presented, to the federal government, claims for payment or approval from Medicare, Medicaid or other government payors that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government, with potential liability including mandatory treble damages and significant per-claim penalties. Manufacturers can be held liable under the federal False Claims Act even when they do not submit claims directly to government payors if they are deemed to “cause” the submission of false or fraudulent claims. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal False Claims Act or federal civil money penalties. The federal False Claims Act also permits a private individual acting as a “whistleblower” to bring actions on behalf of the federal government alleging violations of the federal False Claims Act and to share in any monetary recovery;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which prohibits, among other things, knowingly and willfully executing, or attempting to execute, a scheme or artifice to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e.g., public or private), and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false, fictitious or fraudulent statements in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare benefits, items or services relating to healthcare matters. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- the U.S. Physician Payments Sunshine Act and its implementing regulations, which requires certain manufacturers of drugs, devices, biologics and medical supplies that are reimbursable under Medicare, Medicaid, or the Children’s Health Insurance Program, with specific exceptions, to report annually to CMS information related to certain payments and other transfers of value to physicians (currently defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain non-physician practitioners (nurse practitioners, certified nurse anesthetists, physician assistants, clinical nurse specialists, anesthesiology assistants and certified nurse midwives) as well as teaching hospitals. Manufacturers are also required to disclose ownership and investment interests held by physicians and their immediate family members;
- federal government price reporting laws, which require us to calculate and report complex pricing metrics in an accurate and timely manner to government programs; and
- federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm customers.

Additionally, we are subject to state and foreign equivalents of each of the healthcare laws and regulations described above, 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 European Union. 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 UK. Infringement of these laws could result in substantial fines and imprisonment. EU Directive 2001/83/EC, which is the EU Directive governing medicinal products for human use, further provides that, where medicinal products are being promoted to persons qualified to prescribe or supply them, no gifts, pecuniary advantages or benefits in kind may be supplied, offered or promised to such persons unless they are inexpensive and relevant to the practice of medicine or pharmacy. This provision has been transposed into the Human Medicines Regulations 2012 and so remains applicable in the UK despite its departure from the EU.

Payments made to physicians in certain European Union 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 European Union Member States. These requirements are provided in the national laws, industry codes or professional codes of conduct applicable in the European Union 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 United States 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. In particular, in 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively, the ACA, was enacted, which, among other things, subjected biologic products to potential competition by lower-cost biosimilars; addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected; increased the minimum Medicaid rebates owed by most manufacturers under the Medicaid Drug Rebate Program; extended the Medicaid Drug Rebate program to utilization of prescriptions of individuals enrolled in Medicaid managed care organizations; subjected manufacturers to new annual fees and taxes for certain branded prescription drugs; created a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 70% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D; and provided incentives to programs that increase the federal government's comparative effectiveness research.

In addition, other legislative changes have been proposed and adopted since the ACA was enacted:

- The U.S. Budget Control Act of 2011, among other things, included aggregate reductions of Medicare payments to providers of 2% per fiscal year through 2030.
- The American Taxpayer Relief Act of 2012 became law, which, among other things, reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws 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.
- The U.S. American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several types of providers.
- The American Rescue Plan Act of 2021 into law, which eliminates the statutory Medicaid drug rebate cap, currently set at 100% of a drug's average manufacturer price, for single source and innovator multiple source drugs, beginning January 1, 2024.
- The Inflation Reduction Act of 2022 or IRA includes several provisions that will impact our business to varying degrees, including provisions that reduce the out-of-pocket cap for Medicare Part D beneficiaries to \$2,000 starting in 2025, impose new manufacturer financial liability on all drugs in Medicare Part D, allow the U.S. government to negotiate Medicare Part B and Part D price caps for certain high-cost drugs and biologics without generic or biosimilar competition, require companies to pay rebates to Medicare for certain drug prices that increase faster than inflation, and delay the rebate rule that would limit the fees that pharmacy benefit managers can charge. Further, under the IRA, orphan drugs are exempted from the Medicare drug price negotiation program, but only if they have one rare disease designation and for which the only approved indication is for that disease or condition. If a product receives multiple rare disease designations or has multiple approved indications, it will not qualify for the orphan drug exemption. The effects of the IRA on our business and the healthcare industry in general are not yet known.

Additionally, there has been increasing legislative and enforcement interest in the United States with respect to drug pricing practices. Specifically, there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several U.S. Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, and review the relationship between pricing and manufacturer patient programs.

At 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 expect that the ACA, as well as other healthcare reform measures that may be adopted in the future, may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, lower reimbursement, and new payment methodologies. This could lower the price that we receive for 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 European Union and other jurisdictions, provide accurate information to the FDA, the European Commission and other regulatory authorities, comply with healthcare fraud and abuse laws and regulations in the United States and abroad, report financial information or data accurately, or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, 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 United States and require us to develop and implement costly compliance programs.

We are subject to numerous laws and regulations in each jurisdiction outside the United States 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 United States to comply with certain accounting provisions requiring the company to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations. 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 United States, 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 United States embargoed countries or sanctioned countries, governments, persons and entities. Our expansion outside of the United States 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 United States, which could limit our growth potential and increase our development costs. The failure to comply with laws governing international business practices may result in substantial 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 EEA, is subject to the GDPR, as well as national data protection laws in effect in the member states of the EEA. The GDPR imposes stringent requirements on companies that process personal data, including requirements relating to processing health-related and other sensitive data, 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, 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 and it imposes rules relating to informed consent practices and for clinical trials and notices for clinical trial subjects and investigators. In addition, the GDPR 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. It also provides that EEA member states may make their own laws and regulations limiting the processing of personal data, including genetic, biometric or health data. Noncompliant companies face significant fines, which can be up to 4% of global revenues or €20 million, whichever is greater. Further, from January 1, 2021, companies have had to comply with the GDPR and also the United Kingdom GDPR, or the UK GDPR, which, together with the amended UK Data Protection Act 2018, retains the GDPR in UK national law. The UK GDPR mirrors the fines under the GDPR, i.e., fines up to the greater of €20 million (£17.5 million) or 4% of global turnover. The UK GDPR is currently largely in line with the GDPR, but the data protection regimes may diverge more in the future.

Among other requirements, the GDPR and UK GDPR regulate transfers of personal data subject to the GDPR to third countries that have not been found to provide adequate protection to such personal data, including the United States. Switzerland has also adopted similar restrictions on transfer of personal data outside of its borders. In July 2020, the Court of Justice of the EU, or the CJEU, limited how organizations could lawfully transfer personal data from the EU/EEA to the United States by invalidating the Privacy Shield, which was the main mechanism to transfer personal data to the United States, and imposing further restrictions on the use of standard contractual clauses or SCCs. The European Commission issued revised SCCs on June 4, 2021 to account for the decision of the CJEU and recommendations made by the European Data Protection Board. The new SCCs apply only to the transfer of personal data outside of the EEA and not the UK. The UK's Information Commissioner's Office has also published new data transfer standard contracts for transfers from the UK under the UK GDPR. The European Commission has adopted an adequacy decision in favor of the United Kingdom, enabling data transfers from EU member states to the United Kingdom without additional safeguards. However, the UK 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. In September 2021, the UK government has announced wide-ranging reform of UK data protection laws following Brexit, but these plans have been put on hold. There is a risk that any material changes which are made to the UK data protection regime could result in the European Commission reviewing the UK adequacy decision, and the UK losing its adequacy decision if the European Commission deems the UK to no longer provide adequate protection for 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.

If we are unable to implement a valid solution for personal data transfers from the EEA, United Kingdom or Switzerland, including, for example, obtaining individuals' explicit consent to transfer their personal data from the EEA, United Kingdom, and Switzerland to the United States 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, United Kingdom 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, United Kingdom, 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 changes in 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, UK 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 United States. 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, effective starting on January 1, 2023, the California Privacy Rights Act, or the CPRA, will significantly modify the CCPA, including by expanding consumers' rights with respect to certain sensitive personal information. The CPRA also creates a new state agency that will be vested with authority to implement and enforce the CCPA and the CPRA. Many other states are considering similar legislation, and a broad range of legislative measures also have been introduced at the federal level.

Further, regulations promulgated pursuant to HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or collectively 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. 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. We also face a threat of 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.

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 United States, 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 abbreviated new drug applications, or ANDAs, in the United States. 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 new chemical entity, or 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 new chemical entities 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. 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 (deflazacort) is an FDA-approved corticosteroid marketed by PTC. People with DMD also use prednisone or prednisolone off-label. In addition, there are four FDA-approved exon skipping drugs: EXONDYS 51 (Eteplirsen), VYONDYS 53 (Golodirsen) and AMONDYS 45 (Casimersen), which are naked phosphorodiamidate morpholino oligonucleotides, or PMOs, approved for the treatment of DMD patients amenable to exon 51, exon 53 and exon 45 skipping, respectively, and are marketed by Sarepta, VILTEPSO (Viltolarsen), a naked PMO approved for the treatment of DMD patients amenable to exon 53 skipping, which is marketed in the United States by NS Pharma. Companies focused on developing treatments for DMD that target dystrophin, as our DMD program does, include Sarepta with SRP-5051, a peptide-linked PMO currently being evaluated in a Phase 2 clinical trial for patients amenable to exon 51 skipping, Dyne with DYNE-251, an antibody fragment-conjugated PMO that targets exon 51 skipping and is currently in clinical development, BioMarin Pharmaceutical Inc. with BMN-351, a phosphorothioate oligonucleotide that targets exon 51 skipping and is currently in preclinical development, Wave Life Sciences Ltd. with WVE-N531, a stereopure oligonucleotide in Phase 1/2 clinical development for patients amenable to exon 53 skipping, Daiichi Sankyo with DS-5141b, an exon skipping approach for exon 45 in clinical development, PTC with ataluren, a small molecule targeting nonsense mutations in a Phase 3 clinical trial, Nippon Shinyaku with NS-089/NCNP-02, an oligonucleotide that targets exon 44 skipping that is currently in clinical development, Avidity Biosciences, Inc., which is in clinical development with AOC 1044, an antibody oligonucleotide conjugate that targets exon 44 skipping, and Entrada Therapeutics, Inc., which is in preclinical development with ENTR-601-44, a peptide oligonucleotide conjugate that targets exon 44 skipping and with a clinical hold placed on its investigational new drug application (IND) by the FDA prior to dosing of the first healthy volunteer. In addition, several companies are developing gene therapies to treat DMD, including Pfizer Inc. (PF-06939926), which is currently being assessed in a Phase 3 clinical trial, Sarepta (SRP-9001 and Galgt2 gene therapy program), the former of which is currently being assessed in a Phase 3 clinical trial and for which a BLA has recently been submitted, Solid Biosciences Inc. (SGT-003), currently in preclinical development and REGENXBIO Inc (RGX-202), which has received IND clearance for a Phase 1/2 clinical trial. Gene editing treatments that are in preclinical development are also being pursued by Vertex, Sarepta and Eli Lilly. We are also aware of several companies targeting non-dystrophin mechanisms for the treatment of DMD, including Edgewise Therapeutics with EDG-5506, a muscle stabilizer that is currently in clinical development.

There are currently no approved therapies to treat the underlying cause of DM1. Product candidates currently in development to treat DM1 include: tideglusib, a GSK3- β inhibitor in late-stage clinical development by AMO Pharma Ltd. for the congenital phenotype of DM1; AOC 1001, an antibody linked siRNA in Phase 1/2 clinical development by Avidity Biosciences, Inc.; DYNE-101, an antibody conjugated antisense oligonucleotide in clinical development by Dyne; a microRNA small molecule approach by Arthex Biotech; gene editing treatments in preclinical development by Vertex; an artificial site-specific RNA endonuclease gene therapy being developed by Enzerna Biosciences; an RNA-targeting gene therapy in preclinical development by Locana; an approach by Design Therapeutics to prevent formation of CUG hairpins; an approach utilizing the interaction of small molecules with RNA in preclinical development by Expansion Therapeutics; ENTR-701, a peptide-conjugated PMO in preclinical development by Entrada Therapeutics; and therapeutics based on biomolecular condensate biology in preclinical development by Dewpoint Therapeutics.

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 Pharmaceuticals, Aro Biotherapeutics, Arrowhead Pharmaceuticals, Avidity Biosciences, Dicerna Pharmaceuticals (acquired by Novo Nordisk), Dyne, Entrada Therapeutics, Ionis Pharmaceuticals, NeuBase Therapeutics, PYC Therapeutics 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 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 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 may prove to be inaccurate. Even if the markets in which we compete meet the size estimates and 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 United States and markets in other countries, patients generally rely on third-party payors to reimburse all or part of the costs associated with their treatment. Adequate coverage and reimbursement from governmental healthcare programs, such as Medicare and Medicaid, and commercial payors is critical to new product acceptance. Our ability to successfully commercialize our product candidates will depend in part on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers and other organizations. 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.

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 United States, 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 European Union may be more conservative than CMS. Factors payors consider in determining coverage 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 United States. 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 United States, international operations are generally subject to extensive governmental price controls and other market regulations, and we believe the increasing emphasis on cost-containment initiatives in Europe, 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 European Union, 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 United States. 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 United States, the reimbursement for our product candidates may be reduced compared with the United States 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 United States and other jurisdictions. We and our licensors have sought, and will seek, to protect our proprietary position by filing additional patent applications in the United States and abroad related to certain technologies and our platform that are important to our business. However, our patent portfolio is at an early stage; except for one issued patent and seven applications currently under examination, which we in-licensed from Oxford University and the Medical Research Council of United Kingdom Research and Innovation, substantive examination 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 Patent Cooperation Treaty, or 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 United States 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 United States and other jurisdictions are typically not published until 18 months after filing or, in some cases, not at all. Therefore, we cannot know 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 United States 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 United States, 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

Oxford University Innovation Limited, or OUI, and the Medical Research Council of United Kingdom Research and Innovation, or MRC, to certain patent rights and know-how of OUI and MRC, or the OUI/MRC License. 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 United States could be less extensive than those in the United States. 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 United States. 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 United States. 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 United States and, as a result, may not be able to prevent third parties from practicing our and our licensors' inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. 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 United States. 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 United States 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 United States 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 United States and worldwide, including patent reform legislation such as the Leahy-Smith America Invents Act, or the 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 United States, the first to invent the claimed invention was entitled to the patent, while outside the United States, the first to file a patent application was entitled to the patent. After March 2013, under the Leahy-Smith Act, the United States 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 United States and most other countries are confidential for a period of time after filing or until issuance, we cannot be certain that we or our licensors were the first to either (i) file any patent application related to our product candidates or (ii) invent any of the inventions claimed in our or our licensor's patents or patent applications.

The America Invents Act also includes a number of significant changes that affect the way patent applications 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 United States federal courts necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim 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 United States 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 United States 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 United States 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 United States, 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 United States 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 United States 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 United States 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 United States 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 United States 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 Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Amendments to the Federal Food, Drug, and Cosmetic Act, or the FDCA, a company may file an abbreviated new drug application, or 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 United States 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 the 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 United States 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 offer letters 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, 2022, we had 45 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, expand our facilities and continue to recruit and train additional qualified personnel. 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 are actively pursuing new platforms and product candidates in many therapeutic areas and across a wide range of diseases. Successfully developing product candidates for, and fully understanding the regulatory and manufacturing pathways to, all 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 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.

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, 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 security 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 ongoing COVID-19 pandemic, we may also face increased cybersecurity risks due to our reliance on internet technology and the number of our employees who are working remotely, which may create additional opportunities for cybercriminals to exploit vulnerabilities. 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 security breaches that may remain undetected for an extended period. We may be unable to anticipate all types of security threats, or implement preventive measures effective against all such security 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 security incidents. While we do not believe that we have experienced any significant system failure, accident or security breach to date, if such an event were to occur, 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 breach of our information systems or data, the costs associated with the investigation, remediation and potential notification of the 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 security 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 or security breach 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 the Company’s current and projected business operations and its financial condition and results of operations.

Actual 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. For example, on March 10, 2023, Silicon Valley Bank (“SVB”) was closed by the California Department of Financial Protection and Innovation, which appointed the Federal Deposit Insurance Corporation (“FDIC”) as receiver. Similarly, on March 12, 2023, Signature Bank and Silvergate Capital Corp. were each swept into receivership. Although a statement by the Department of the Treasury, the Federal Reserve and the FDIC indicated that all depositors of SVB would have access to all of their money after only one business day of closure, including funds held in uninsured deposit accounts, borrowers under credit agreements, letters of credit and certain other financial instruments with SVB, Signature Bank or any other financial institution that is placed into receivership by the FDIC, may be unable to access undrawn amounts thereunder. Although we are not a borrower or party to any such instruments with SVB, Signature or any other financial institution currently in receivership, 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 SVB credit agreements and arrangements, and third parties such as beneficiaries of letters of credit (among others), may experience direct impacts from the closure of SVB and uncertainty remains over liquidity concerns in the broader financial services industry, including for example in the case of First Republic Bank and Credit Suisse during March 2023. 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 of such 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 immediately 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, or that they would do so in a timely fashion.

Although we assess our banking and customer relationships as we believe necessary or appropriate, our access to funding sources and other credit arrangements in amounts adequate to finance or capitalize our current and projected future business operations could be significantly impaired by factors that affect the Company, the financial institutions with which the Company has credit agreements or 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. These factors could involve financial institutions or financial services industry companies with which the Company has financial or business relationships, but could also include factors involving financial markets or the financial services industry generally.

The results of events or concerns that involve one or more of these factors could include a variety of material and adverse impacts on our current and projected business operations and our financial condition and results of operations. These could include, but may not be limited to, the following:

- Delayed access to deposits or other financial assets or the uninsured loss of deposits or other financial assets;
- Potential or actual breach of statutory, regulatory or contractual obligations, including obligations that require the Company to maintain letters of credit or other credit support arrangements;
- Termination of cash management arrangements and/or delays in accessing or actual loss of funds subject to cash management arrangements.

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 planned business operations, and our current or projected financial condition and results of operations.

In addition, any further deterioration in the macroeconomic economy or financial services industry could lead to losses or defaults by our suppliers, which in turn, could have a material adverse effect on our current and/or planned business operations and our current or projected results of operations and financial condition. For example, a customer may fail to make payments when due, default under their agreements with us, become insolvent or declare bankruptcy, or a supplier may determine that it will no longer deal with us as a customer. In addition, a customer or supplier could be adversely affected by any of the liquidity or other risks that are described above as factors that could result in material adverse impacts on the Company, including but not limited to delayed access or loss of access to uninsured deposits or loss of the ability to draw on existing credit facilities involving a troubled or failed financial institution. Any customer, collaborator or supplier bankruptcy or insolvency, or the failure of any customer or collaborator to make payments when due, or any breach or default by a customer, collaborator or supplier, or the loss of any significant supplier or collaborator relationships, could result in material losses to the Company and may have a material adverse impact on our business.

The ongoing COVID-19 pandemic may affect our ability to initiate and complete preclinical studies and current or future clinical trials, disrupt regulatory activities, or have other adverse effects on our business and operations. In addition, this pandemic has caused substantial disruption in the financial markets and may adversely impact economies worldwide, which could negatively impact our operations and our ability to raise additional capital.

The ongoing COVID-19 pandemic has broadly affected the global economy and has put a significant strain on healthcare resources. The ultimate extent of the impact of the ongoing COVID-19 pandemic on our business, financial condition and results of operations is highly uncertain. The continuation of the worldwide COVID-19 pandemic may affect our ability to initiate and complete preclinical studies and current or planned clinical trials, disrupt regulatory activities or have other adverse effects on our business, results of operations, financial condition and prospects. In addition, the ongoing COVID-19 pandemic has adversely impacted economies worldwide and has caused substantial disruption in the financial markets, both of which could adversely affect our business, operations and ability to raise funds to support our operations, and may also impact the volatility of our stock price and trading in our stock.

The future progression of the pandemic and its effects on our business and operations remain uncertain. We and our CDMOs and CROs have experienced a reduction in the capacity to undertake research-scale production and to execute some preclinical studies, and we may face disruptions that affect our ability to initiate and complete preclinical studies, and 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 shortages because of ongoing efforts to address the pandemic. Further, since the beginning of the COVID-19 pandemic, several vaccines for COVID-19 have received Emergency Use Authorization by the FDA and a number of those later received marketing approval. Additional vaccines may be authorized or approved in the future. The demand for COVID-19 vaccines and treatments and potential for manufacturing facilities and materials to be commandeered under the Defense Production Act of 1950, or equivalent foreign legislation, may make it more difficult to obtain materials or manufacturing slots for the products needed for our clinical trials, which could lead to delays in these trials. We and our CROs and CDMOs may face disruptions related to our future

IND- or CTA-enabling studies and clinical trials arising from delays in preclinical studies, manufacturing disruptions, and the ability to obtain necessary IRB, IBC or other necessary site approvals, as well as other delays at clinical trial sites.

The response to the ongoing COVID-19 pandemic may also redirect resources with respect to regulatory and intellectual property matters in a way that would adversely impact our ability to progress regulatory approvals and protect our intellectual property. In addition, we may face impediments to regulatory meetings and approvals due to measures intended to limit in-person interactions. We cannot be certain what the overall impact of the ongoing COVID-19 pandemic will be on our business, although for the reasons described above it has the potential to adversely affect our financial condition, results of operations and prospects.

Risks Related to Ownership of Our Common Stock

Prior to the completion of our IPO, there was no public market for 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.

Prior to the completion of our IPO, there was no public market for shares of our common stock. 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 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. 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 may be volatile and fluctuate 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 United States 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 ongoing 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 ongoing COVID-19 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 could disrupt or otherwise adversely impact our operations and those of third parties upon which we rely. Related sanctions, export controls or other actions that have been or may be initiated by nations, including the United States or the European Union, 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 March 15, 2023, our executive officers, directors, greater than five percent shareholders and their affiliates beneficially own approximately 76.8% 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.

A significant portion of our total outstanding shares is subject to restrictions on resale and to the extent such restrictions are lessened or removed, by virtue of the registration of such shares or otherwise, the sale of such currently restricted shares 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. Prior to November 2, 2022, we had 23,361,924 shares of common stock outstanding and 13,363,980 of those shares of common stock were restricted as a result of securities laws or lock-up agreements entered into in connection with our IPO. On November 2, 2022, 4,614,803 shares of these restricted shares became eligible for sale in the public market and 8,743,269 shares of these restricted shares became eligible for sale in the public market subject to certain requirements of Rule 144 promulgated under the Securities Act.

Moreover, 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 a registration statement 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 the lock-up agreements.

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 the 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 will be required to furnish a report by our management on our internal control over financial reporting beginning with our second filing of our Annual Report on Form 10-K with the SEC. 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 amended and restated certificate of incorporation and our 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 the 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 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 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 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 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 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 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 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, 2022, we had federal and state NOL carryforwards of \$0.5 million. The Company did not generate U.K. NOLs in 2022 and does not anticipate any going forward.

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. In 2022, 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 UK 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 UK 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 UK 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. Any future actions regarding transfer of assets from our UK subsidiary or other international subsidiaries could give rise to tax liabilities for us and/or to the erosion of our tax attributes (such as net operating losses).

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 Securities Exchange Act of 1934, as amended, or 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 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 March 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.

In 2022, we primarily operated out of approximately 800 square feet of office space located at 245 Main Street, Cambridge, Massachusetts 02142 and 6,500 square feet of laboratory space at the University of Massachusetts, Mount Ida Campus in Newton, Massachusetts at the School of Applied Sciences Building. The current terms for the office space lease is month-to-month, with a 30-day written notice of cancellation. The lease for our lab space commenced on February 1, 2022 and expired on January 31, 2023.

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, 2022, 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 March 15, 2023, we had 19 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 Annual Report on Form 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 estimated 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, Nicolaus & Company, Incorporated 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.”

We are 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 Enhanced Delivery Oligonucleotide, or EDO, platform is founded on over a decade of research and development and leverages cell-penetrating peptides to improve the uptake and activity of conjugated oligonucleotide therapeutics. This technology was initially developed through a collaboration between researchers at the University of Oxford and the Medical Research Council of United Kingdom Research and Innovation. We have licensed an extensive patent portfolio from these institutions to support the further advancement and potential commercialization of our EDO platform. 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 and the central nervous system, or CNS. We have also seen robust delivery of oligonucleotides to skeletal muscle in a clinical trial. Furthermore, the high levels of pharmacological activity observed in clinical and preclinical studies support our belief that our EDO platform technology has the potential to deliver therapeutic agents to the cell nucleus. Using these EDO peptides, we are generating a pipeline of oligonucleotide product candidates that target the root cause of serious diseases.

We are currently in clinical-stage development and completed a first-in-human Phase 1 clinical trial in healthy volunteers, or HVs, with our lead product candidate, PGN-EDO51, in the third quarter of 2022. We are developing PGN-EDO51 to treat individuals with Duchenne muscular dystrophy, or DMD, whose mutations are amenable to an exon 51-skipping therapeutic approach. An exon is a segment of a gene that – together with other exons – contains the code that is translated into a protein. Exon skipping is a therapeutic modality that enables mutations in the gene to be bypassed, thereby repairing this code and enabling production of a truncated, yet functional version of the target protein. In a Phase 1 clinical trial, treatment with PGN-EDO51 resulted in the highest levels of exon skipping and oligonucleotide delivery in humans following a single dose when compared to publicly available data for other approaches. In non-human primate, or NHP, studies, PGN-EDO51 at a dose of 30 mg/kg achieved over 70% exon 51 skipping in skeletal muscle, including diaphragm, and in mdx mouse studies dystrophin levels of over 80% were observed in skeletal muscle following a single 60 mg/kg dose of PGN-EDO23, the murine analogue of PGN-EDO51. These results represent the highest level of exon 51 skipping in NHP skeletal muscle at tolerable target dose levels, and the highest level of dystrophin production in mdx mice skeletal muscle, when compared to clinical-stage DMD therapeutic candidates. In addition, in head-to-head NHP studies, we observed that PGN-EDO51 had greater activity than R6G-PMO, which we believe to be structurally equivalent to Sarepta Therapeutics, Inc.’s, or Sarepta’s, SRP-5051, the most clinically advanced peptide-antisense oligonucleotide conjugate. Our Phase 1 clinical trial also indicated that PGN-EDO51 was generally well-tolerated at pharmacologically active dose levels. Moving forward, our clinical development program comprises two, parallel Phase 2 studies of PGN-EDO51 in DMD patients whose disease is amenable to an exon 51 skipping approach. The first study, CONNECT1-EDO51, is expected to be an open-label MAD study to open in Canada in the first half of 2023, with initial dystrophin, exon skipping and safety data anticipated in 2024. The second study, CONNECT2-EDO51 is expected to be a global, randomized, double-blind, placebo-controlled MAD clinical trial, or RCT, anticipated to open in the second half of 2023, pending clearance by the U.S. Food and Drug Administration, or FDA, of an Investigational New Drug, or IND, filing, or clearance by the European Medicines Agency, or EMA, of a Clinical Trial Application, or CTA, filing, in either case anticipated in the second half of this year. Learnings from the open label study will inform the conduct of the global RCT which is intended to support a future accelerated approval pathway for PGN-EDO51. Building on the high levels of exon skipping and tissue concentration observed in our Phase 1 trial, we believe that repeat dosing of PGN-EDO51 may lead to the accumulation of exon 51 skipped transcript and dystrophin protein in patients, which may in turn drive meaningful clinical benefit for those who live with this devastating, progressive, life-shortening disease.

We are also developing PGN-EDODM1 for the treatment of myotonic dystrophy type 1, or DM1, and are utilizing what we believe to be a unique mechanism of action. The therapeutic oligonucleotide component of PGN-EDODM1 is engineered to bind to the cytosine-uracil-guanine (CUG) repeat expansion present in the DMPK mRNA of DM1 patients, thus reducing the ability of these trinucleotide repeats to sequester MBNL1, a critical transcription factor. The liberation of MBNL1 in turn leads to the correction of downstream mis-splicing events that are evident in DM1, and thus this approach – which is not designed to knock down DPMK – has the potential to directly address the underlying genetic defect central to this disease. Treatment with PGN-EDODM1 resulted in the robust correction of mis-splicing in preclinical models with both long and short CTG repeats, including in the HSALR mouse model, where complete reversal of myotonia was also observed following a single dose. Furthermore, the oligonucleotide concentrations that were observed to be pharmacologically active in this mouse model of DM1 were found to be comparable to the tissue concentrations

of oligonucleotide in human muscle observed in our clinical trial of PGN-EDO51. We anticipate opening our FREEDOM-DM1 Phase 1, randomized, placebo controlled SAD clinical trial of PGN-EDODM1 in DM1 patients in the first half of 2023, with functional assessments, correction of mis-splicing and safety data anticipated in 2024. Based on data obtained in our Phase 1 HV study of PGN-EDO51, we believe that PGN-EDODM1 has the potential to achieve tissue concentrations in people living with DM1 that could lead to clinically meaningful outcomes.

In addition to these lead candidates, we are developing EDO therapeutics for further DMD exon skipping populations, including exon 53-, 45- and exon 44-skipping amenable patients, and have observed robust exon skipping levels in NHP for our PGN-EDO53 program, and in wild-type human cells for our PGN-EDO45 and PGN-EDO44 programs. We have also initiated research efforts for additional indications, including neuromuscular diseases and neurologic disorders, and from this pipeline of candidates we anticipate advancing additional programs into CTA and IND-enabling studies in 2024.

Initial Public Offering and Liquidity

On May 10, 2022, we closed our initial public offering, or 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 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.

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

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.

We have incurred operating losses in each year since our inception. Our net losses were \$69.1 million and \$27.3 million for the years ended December 31, 2022 and December 31, 2021, respectively. As of December 31, 2022, we had cash and cash equivalents of \$181.8 million. As of December 31, 2022, we had an accumulated deficit of \$102.9 million. We expect our expenses and operating losses will continue to increase 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 and current and planned clinical trials and our expenditures on other research and development activities.

Based upon our current operating plans, we believe that the estimated net proceeds of our IPO, together with our existing cash and cash equivalents, will be sufficient to fund our currently planned operations into early 2025. 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.

Impact of COVID-19 on our Business

The global coronavirus disease 2019, or COVID-19, pandemic continues to evolve, and we continue to monitor the COVID-19 situation. The extent of the impact of the ongoing COVID-19 pandemic on our business, operations and clinical development timelines and plans remains uncertain, and will depend on certain developments, including the duration and spread of the pandemic and its impact on contract research organizations, or CROs, third-party manufacturers, and other third parties with whom we do business, as well as its impact on regulatory authorities and our key scientific and management personnel. To the extent possible, we are conducting business as usual, with only advisable modifications to employee travel. We continue to actively monitor the impacts of COVID-19 and may take further actions that alter our operations, including those that may be required by federal, state or local authorities, or that we determine are in the best interests of our employees and other third parties with whom we do business. The extent to which the ongoing COVID-19 pandemic may affect our business, operations and clinical development timelines and plans, including the resulting impact on our expenditures and capital needs, remains uncertain and is subject to change.

Corporate Reorganization

We were initially formed as PepGen Limited on January 25, 2018, in the United Kingdom. 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 the year at PepGen Limited.

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 contract research organizations, or CROs, contract development manufacturers or 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. Research and development expenses are presented net of reimbursement received related to a U.K. grant and refundable research and development tax credits from the U.K. government. In 2022, 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.

The following table summarizes our research and development expenses for the year ended December 31, 2022 and December 31, 2021, respectively. 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 typically deployed across multiple programs. As such, we do not track internal expenses on a program-specific basis.

	Year Ended December 31,	
	2022	2021
External expenses:		
PGN-EDO51	\$ 21,089	\$ 12,888
PGN-EDODM1	10,853	1,691
PGN-EDO53	2,990	45
Other programs and unallocated expenses	2,306	202
Total external expense	37,238	14,826
Internal expenses:		
Personnel-related (including stock-based compensation)	10,744	2,960
Other	6,095	1,213
Total research and development expenses	<u>\$ 54,077</u>	<u>\$ 18,999</u>

We plan to continue to increase our research and development expenses in 2023 as we continue to conduct our ongoing research and development activities, advance our preclinical research programs toward clinical development, including conducting IND- and CTA-enabling studies, and conducting clinical trials for PGN-EDO51 and PGN-EDODM1. 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:

- clinical trials, 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;
- 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 accounting and consulting services, and insurance costs.

We anticipate that our general and administrative expenses will increase in 2023 to support our continued research and development activities. We also anticipate increased expenses related to 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 costs associated with operating as a public company.

Other Income (Expense), Net

Interest income

Interest income consists of interest earned on our cash deposits.

Other income (expense)

We classified our outstanding warrants to purchase shares of our Series A-2 convertible preferred stock as liabilities on our consolidated balance sheets at their estimated fair value as the underlying convertible preferred stock is classified as temporary equity. At the end of each reporting period, changes in the estimated fair value during the period were recorded as a component of other income (expense), net. We recognized changes in the fair value of our warrant liability until the warrants were exercised on May 4, 2022, prior to the completion of our IPO.

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

Income Taxes

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. During the year ended December 31, 2022, we recorded a \$3.7 million tax charge associated with the transfer of our intellectual property assets from our wholly owned subsidiary, PepGen Limited, to the parent company, PepGen Inc. (see Note 11 of Notes to the Consolidated Financial Statements).

Results of Operations

Comparison of the Year Ended December 31, 2022 and 2021

The following table summarizes our results of operations for the year ended December 31, 2022 and 2021 (in thousands):

	Year Ended December 31,		Period-to- Period Change
	2022	2021	
Operating expenses:			
Research and development	\$ 54,077	\$ 18,999	\$ 35,078
General and administrative	14,224	8,110	6,114
Total operating expenses	\$ 68,301	\$ 27,109	\$ 41,192
Operating loss	\$ (68,301)	\$ (27,109)	\$ 41,192
Other income (expense), net			
Interest income	2,793	—	2,793
Other income (expense), net	110	(172)	282
Total other income (expense), net	2,903	(172)	3,075
Net loss before income tax	\$ (65,398)	\$ (27,281)	\$ (38,117)
Income tax expense	(3,706)	—	(3,706)
Net loss	\$ (69,104)	\$ (27,281)	\$ (41,823)

Research and Development Expenses

Research and development expenses increased by \$35.1 million from \$19.0 million for the year ended December 31, 2021, to \$54.1 million for the year ended December 31, 2022. This increase was attributable to increased research and development activities related to the advancement of our pipeline programs, including a \$15.5 million increase in preclinical and manufacturing costs, a \$2.9 million increase in clinical costs due to our Phase 1 trial for PGN-EDO51, and a \$7.6 million increase in personnel-related costs due to increased headcount, including an increase of \$1.3 million in stock-based compensation expense. There was also an increase of \$4.7 million in research and development tax credits recognized as an offset to research and development expense during the year ended December 31, 2021, and a \$1.7 million increase in other research and development expense primarily related to the \$1.4 million OUI exit fee that was expensed upon completion of our IPO (see Note 2 of Notes to Consolidated Financial Statements).

General and Administrative Expenses

General and administrative expenses increased by \$6.1 million from \$8.1 million for the year ended December 31, 2021, to \$14.2 million for the year ended December 31, 2022. The increase was primarily driven by a \$2.7 million increase in personnel-related costs due to increased headcount, including an increase of \$1.9 million in stock-based compensation expense, an increase of \$2.2 million in legal, accounting, consulting, and insurance costs associated operating as a public company costs, and a \$1.2 million increase in facility-related costs due to our expansion of operations in Boston, Massachusetts.

Other Income (Expense), Net

Other income (expense), net was income of \$2.9 million for the year ended December 31, 2022 compared to expense of \$0.2 million for the year ended December 31, 2021. The increase was primarily driven by interest earned from our cash deposits.

Income Tax Expense

Income tax expense increased by \$3.7 million from nil for the year ended December 31, 2021, to \$3.7 million for the year ended December 31, 2022 due to the transfer of all intellectual property assets from PepGen Limited to the parent company, PepGen Inc., pursuant to an asset transfer agreement, effective January 1, 2022. The transfer of the intellectual property assets resulted in an estimated tax charge to His Majesty's Revenue & Customs, after considering net operating loss carryforwards, of \$3.7 million, inclusive of the \$0.8 million uncertain tax position. The liability for the estimated tax accounted for in accrued expenses on the consolidated balance sheet and was \$3.2 million as of December 31, 2022 after currency translation.

Liquidity and Capital Resources

Sources of Liquidity

From our inception in January 2018 through December 31, 2022, we have funded our operations primarily through the sale of our common stock and convertible preferred stock. We have received aggregate gross proceeds of \$163.9 million from these sales. Additionally, we received gross proceeds from our IPO of \$108.0 million, and \$14.9 million when the underwriters partially exercised their option to purchase 1,350,000 additional shares of common stock.

Future Funding Requirements

As of December 31, 2022 we had cash and cash equivalents in the amount of \$181.8 million, which includes net proceeds of \$110.2 million from our IPO. Based on our current operating plans, we believe that our existing cash and cash equivalents will be sufficient to fund our operations into early 2025. 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 type, number, scope, progress, expansions, results, costs, and timing of, discovery, preclinical studies and clinical trials of our product candidates which we are pursuing or may choose to pursue in the future;
- the costs and timing of manufacturing for our product candidates and commercial manufacturing if any product candidate is approved;

- the costs, timing, and outcome of regulatory review of our product candidates;
- the terms and timing of establishing and maintaining licenses and other similar arrangements;
- the legal costs of obtaining, maintaining, and enforcing our patents and other intellectual property rights;
- our efforts to enhance operational systems and hire additional personnel to satisfy our obligations as a public company;
- the costs associated with hiring additional personnel and consultants as our preclinical and clinical activities increase;
- the costs and timing of establishing or securing sales and marketing capabilities if any product candidate is approved;
- our ability to achieve sufficient market acceptance, coverage and adequate reimbursement from third-party payors and adequate market share and revenue for any approved products;
- costs associated with any products or technologies that we may in-license or acquire; and
- costs associated with short-term leases and the lease of lab in office space commenced in early 2022.

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 year ended December 31, 2022 and December 31, 2021 (in thousands):

	Years Ended December 31,	
	2022	2021
Net cash (used in) provided by:		
Operating activities	\$ (59,265)	\$ (22,599)
Investing activities	(3,755)	(500)
Financing activities	112,193	147,656
Effect of exchange rate changes on cash	(316)	33
Net increase in cash, cash equivalents and restricted cash	<u>\$ 48,857</u>	<u>\$ 124,590</u>

Operating Activities

For the year ended December 31, 2022, net cash used in operating activities was \$59.3 million resulting from our net loss of \$69.1 million partially offset by cash provided by changes in our operating assets and liabilities of \$4.5 million and non-cash charges of \$5.3 million. The net changes in our operating assets and liabilities were primarily due to an increase in accrued expenses of \$5.5 million and receipt of \$4.2 million associated with our U.K. R&D tax credit in 2022, which is accounted for in other receivables. These increases were partially offset by a \$2.0 million decrease in operating lease liabilities related to cash paid towards tenant improvements on our new office and lab lease. Non-cash charges included \$4.8 million in share-based compensation expense and \$0.5 million in depreciation expense.

For the year ended December 31, 2021, net cash used in operating activities was \$22.6 million resulting from our net loss of \$27.3 million partially offset by cash provided by changes in our operating assets and liabilities of \$2.8 million and non-cash charges of \$1.9 million. The net changes in our operating assets and liabilities were primarily due to increases in accrued expenses and accounts payable of \$9.3 million, partially offset by increases in other receivables and prepaids and other current and non-current

assets of \$6.6 million. This is primarily driven by the \$3.5 million U.K. tax credit which was recorded as a receivable at year-end. The non-cash charges included \$1.5 million of stock-based compensation, \$0.2 million of depreciation expense and \$0.2 million from the change in the fair value of preferred stock warrant liability.

Investing Activities

Net cash used in investing activities was \$3.8 million during the year ended December 31, 2022 as compared to \$0.5 million during the year ended December 31, 2021. Cash used for investing activities was related to the purchase of property and equipment.

Financing Activities

Net cash provided by financing activities was \$112.2 million for the year ended December 31, 2022, which was primarily the result of \$114.3 million in net proceeds from the Company's IPO, after deducting the payment of \$2.7 million in IPO-related costs made in 2022. In 2021, the Company made payments of \$1.4 million in IPO-related costs. Total net proceeds from the IPO were \$110.2 million. Additionally, the Company generated \$0.4 million from the exercise of the A-2 preferred stock warrants and \$0.2 million in proceeds from stock option exercises.

Net cash provided by financing activities was \$147.7 million for the year ended December 31, 2021. The increase in net cash provided by financing activities was primarily due to the proceeds of \$37.0 million raised from the sale of our Series A-2 convertible preferred stock and the proceeds of \$112.1 million from the sale of our Series B convertible preferred stock partially offset by \$1.4 million in deferred offering costs related to our IPO.

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 United States, or GAAP. The preparation of our financial statements requires us to make estimates and management discussion 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, CMOs, 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 FASB ASC Topic 718, *Compensation—Stock Compensation* (ASC 718). 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 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 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* (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.

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 Annual Report for the year ended December 31, 2022.

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

Our management, under the supervision and with the participation of our Chief Executive Officer and Chief Financial Officer (our principal executive officer and principal financial officer, respectively), evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2022. The term "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act means controls and other procedures of an issuer that are designed to ensure that information required to be disclosed by an issuer in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by an issuer in the reports that it files or submits under the Exchange Act is accumulated and communicated to the issuer's management, including its principal executive and principal financial officers, or persons performing similar functions, as appropriate to allow timely decisions regarding required disclosure.

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. Based on the evaluation of our disclosure controls and procedures as of December 31, 2022, our Chief Executive Officer and Chief Financial Officer concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

Management's Annual Report on Internal Control Over Financial Reporting

This Annual Report does not include a report of management's assessment regarding internal control over financial reporting or an attestation report of the company's registered public accounting firm due to a transition period established by rules of the Securities and Exchange Commission for newly public 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, 2022 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information.

The Company recently entered into new employment agreements with each of James McArthur, Ph.D., Noel Donnelly, M.B.A., Jaya Goyal, Ph.D., Michelle L. Mellion, M.D. and Niels Svenstrup, Ph.D. (each, an "executive"), which agreements supersede any prior offer letters or employment agreements previously entered into. These new agreements were authorized by our compensation committee.

James McArthur, Ph.D.

On March 21, 2023, we entered into an employment agreement, or the McArthur Employment Agreement, with Dr. McArthur, to continue to be employed as our Chief Executive Officer. The McArthur Employment Agreement provides for Dr. McArthur's annual base salary, a discretionary annual bonus, and his ability to participate in our benefit plans generally. Dr. McArthur's target bonus is equal to 50% of his annual base salary.

In the event of a termination of Dr. McArthur's employment by the Company without "cause" or Dr. McArthur's resignation for "good reason" (each as defined in the McArthur Employment Agreement), subject to Dr. McArthur's execution of the Separation Agreement and Release (as defined in McArthur Employment Agreement) and the Separation Agreement and Release becoming fully effective, the Company will pay Dr. McArthur (i) a severance amount equal to 12 months of his base salary, (ii) subject to Dr. McArthur's election to receive continued health benefits under COBRA, payment of premiums for participation in our health benefit plans (or cash payments equal to the amount of such premiums) for up to twelve (12) months and (iii) prorated target bonus for the year in which the termination occurs. In addition, in the event that such a termination occurs within twelve (12) months following the effective date of a "Sale Event" (as defined in the Company's applicable equity plans), subject to Dr. McArthur's execution of the Separation Agreement and Release and the Separation Agreement and Release becoming fully effective, the Company will pay Dr. McArthur (i) a severance amount equal to 18 months of his base salary, (ii) subject to Dr. McArthur's election to receive continued health benefits under COBRA, payment of premiums for participation in our health benefit plans (or cash payments equal to the amount of such premiums) for up to eighteen (18) months and (iii) the target bonus for the year in which the termination occurs, and any unvested equity awards held by the executive immediately prior to the executive's termination date will be deemed immediately vested effective as of the termination date.

Noel Donnelly, M.B.A.

On March 21, 2023, we entered into an employment agreement, or the Donnelly Employment Agreement, with Mr. Donnelly, to continue to be employed as our Chief Financial Officer. The Donnelly Employment Agreement provides for Mr. Donnelly's annual base salary, a discretionary annual bonus and his ability to participate in our benefit plans generally. Mr. Donnelly's target bonus is equal to 40% of his annual base salary.

In the event of a termination of Mr. Donnelly's employment by the Company without "cause" or his resignation for "good reason" (each as defined in the Donnelly Employment Agreement), subject to Mr. Donnelly's execution of the Separation Agreement and Release (as defined in Donnelly Employment Agreement) and the Separation Agreement and Release becoming fully effective, the Company will pay Mr. Donnelly (i) a severance amount equal to nine (9) months of his base salary, (ii) subject to Mr. Donnelly's election to receive continued health benefits under COBRA, payment of premiums for participation in our health benefit plans (or cash payments equal to the amount of such premiums) for up to nine (9) months and (iii) prorated target bonus for the year in which the termination occurs. In addition, in the event that such a termination occurs within twelve (12) months following the effective date of a "Sale Event" (as defined in the Company's applicable equity plans), subject to Mr. Donnelly's execution of the Separation Agreement and Release and the Separation Agreement and Release becoming fully effective, the Company will pay Mr. Donnelly (i) a severance amount equal to twelve (12) months of his base salary, (ii) subject to Mr. Donnelly's election to receive continued health benefits under COBRA, payment of premiums for participation in our health benefit plans (or cash payments equal to the amount of such premiums) for up to twelve (12) months and (iii) the target bonus for the year in which the termination occurs, and any unvested

equity awards held by the executive immediately prior to the executive's termination date will be deemed immediately vested effective as of the termination date.

Jaya Goyal, Ph.D.

On March 21, 2023, we entered into an employment agreement, or the Goyal Employment Agreement, with Dr. Goyal, to continue to be employed as the Executive Vice President, Research and Preclinical Development. The Goyal Employment Agreement provides for Goyal's annual base salary, a discretionary annual bonus and her ability to participate in our benefit plans generally. Dr. Goyal's target bonus is equal to 40% of her annual base salary.

In the event of a termination of Dr. Goyal's employment by the Company without "cause" or Dr. Goyal's resignation for "good reason" (each as defined in the Goyal Employment Agreement), subject to Dr. Goyal's execution of the Separation Agreement and Release (as defined in Goyal Employment Agreement) and the Separation Agreement and Release becoming fully effective, the Company will pay Dr. Goyal (i) a severance amount equal to nine (9) months of her base salary, (ii) subject to Dr. Goyal's election to receive continued health benefits under COBRA, payment of premiums for participation in our health benefit plans (or cash payments equal to the amount of such premiums) for up to nine (9) months and (iii) prorated target bonus for the year in which the termination occurs. In addition, in the event that such a termination occurs within twelve (12) months following the effective date of a "Sale Event" (as defined in the Company's applicable equity plans), subject to Dr. Goyal's execution of the Separation Agreement and Release and the Separation Agreement and Release becoming fully effective, the Company will pay Dr. Goyal (i) a severance amount equal to twelve (12) months of his base salary, (ii) subject to Dr. Goyal's election to receive continued health benefits under COBRA, payment of premiums for participation in our health benefit plans (or cash payments equal to the amount of such premiums) for up to twelve (12) months and (iii) the target bonus for the year in which the termination occurs, and any unvested equity awards held by the executive immediately prior to the executive's termination date will be deemed immediately vested effective as of the termination date.

Michelle L. Mellion, M.D.

On March 21, 2023, we entered into an employment agreement, or the Mellion Employment Agreement, with Dr. Mellion, to continue to be employed as the Executive Vice President, Research and Preclinical Development. The Mellion Employment Agreement provides for Mellion's annual base salary, a discretionary annual bonus and her ability to participate in our benefit plans generally. Dr. Mellion's target bonus is equal to 35% of her annual base salary.

In the event of a termination of Dr. Mellion's employment by the Company without "cause" or Dr. Mellion's resignation for "good reason" (each as defined in the Mellion Employment Agreement), subject to Dr. Mellion's execution of the Separation Agreement and Release (as defined in Mellion Employment Agreement) and the Separation Agreement and Release becoming fully effective, the Company will pay Dr. Mellion (i) a severance amount equal to nine (9) months of her base salary, (ii) subject to Dr. Mellion's election to receive continued health benefits under COBRA, payment of premiums for participation in our health benefit plans (or cash payments equal to the amount of such premiums) for up to nine (9) months and (iii) prorated target bonus for the year in which the termination occurs. In addition, in the event that such a termination occurs within twelve (12) months following the effective date of a "Sale Event" (as defined in the Company's applicable equity plans), subject to Dr. Mellion's execution of the Separation Agreement and Release and the Separation Agreement and Release becoming fully effective, the Company will pay Dr. Mellion (i) a severance amount equal to twelve (12) months of his base salary, (ii) subject to Dr. Mellion's election to receive continued health benefits under COBRA, payment of premiums for participation in our health benefit plans (or cash payments equal to the amount of such premiums) for up to twelve (12) months and (iii) the target bonus for the year in which the termination occurs, and any unvested equity awards held by the executive immediately prior to the executive's termination date will be deemed immediately vested effective as of the termination date.

Niels Svenstrup, Ph.D.

On March 21, 2023, we entered into an employment agreement, or the Svenstrup Employment Agreement, with Dr. Svenstrup, to continue to be employed as the Executive Vice President, Research and Preclinical Development. The Svenstrup Employment Agreement provides for Svenstrup's annual base salary, a discretionary annual bonus and her ability to participate in our benefit plans generally. Dr. Svenstrup's target bonus is equal to 35% of his annual base salary.

In the event of a termination of Dr. Svenstrup's employment by the Company without "cause" or Dr. Svenstrup's resignation for "good reason" (each as defined in the Svenstrup Employment Agreement), subject to Dr. Svenstrup's execution of the Separation Agreement and Release (as defined in Svenstrup Employment Agreement) and the Separation Agreement and Release becoming fully effective, the Company will pay Dr. Svenstrup (i) a severance amount equal to nine (9) months of her base salary, (ii) subject to Dr. Svenstrup's election to receive continued health benefits under COBRA, payment of premiums for participation in our health benefit plans (or cash payments equal to the amount of such premiums) for up to nine (9) months and (iii) prorated target bonus for the year in

which the termination occurs. In addition, in the event that such a termination occurs within twelve (12) months following the effective date of a “Sale Event” (as defined in the Company’s applicable equity plans), subject to Dr. Svenstrup’s execution of the Separation Agreement and Release and the Separation Agreement and Release becoming fully effective, the Company will pay Dr. Svenstrup (i) a severance amount equal to twelve (12) months of his base salary, (ii) subject to Dr. Svenstrup’s election to receive continued health benefits under COBRA, payment of premiums for participation in our health benefit plans (or cash payments equal to the amount of such premiums) for up to twelve (12) months and (iii) the target bonus for the year in which the termination occurs, and any unvested equity awards held by the executive immediately prior to the executive’s termination date will be deemed immediately vested effective as of the termination date.

The foregoing description of the employment agreements is not complete and is qualified in its entirety by reference to the complete text of each such agreement, copies of which are filed as Exhibits 10.7, 10.8, 10.9, 10.10 and 10.11 hereto and are incorporated herein by reference.

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 the Company's definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the close of the Company's fiscal year ended December 31, 2022.

Item 11. Executive Compensation.

The information required under this item is incorporated herein by reference to the Company's definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the close of the Company's fiscal year ended December 31, 2022.

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 the Company's definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the close of the Company's fiscal year ended December 31, 2022.

Item 13. Certain Relationships and Related Transactions, and Director Independence.

The information required under this item is incorporated herein by reference to the Company's definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the close of the Company's fiscal year ended December 31, 2022.

Item 14. Principal Accounting Fees and Services.

The information required under this item is incorporated herein by reference to the Company's definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the close of the Company's fiscal year ended December 31, 2022.

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 Annual Report on Form 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 of the Company (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 of the Company (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***	Amended and Restated By-laws of the Company (Incorporated by reference to Exhibit 3.2 to the Company's Quarterly Report on Form 10-Q filed on June 16, 2022 (File No. 001-41374)).
4.1***	Amended and Restated Investors' Rights Agreement, dated July 30, 2021, among the Registrant 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
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 (Incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q filed on November 10, 2022 (File No. 001-41374)).
10.6***	Form of Indemnification Agreement between Registrant 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 Registrant
10.8*	Employment Agreement, dated March 21, 2023, between Noel Donnelly and the Registrant
10.9*	Employment Agreement, dated March 21, 2023, between Jaya Goyal and the Registrant
10.10*	Employment Agreement, dated March 21, 2023, between Michelle Mellion and the Registrant
10.11*	Employment Agreement, dated March 21, 2023, between Niels Svenstrup and the Registrant
10.12***	License of Technology, dated November 23, 2020, among Oxford University Limited, Medical Research Council 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)).
10.13***	Lease, dated December 1, 2021, between B9 LS Harrison & Washington LLC and the Registrant (Incorporated by reference to Exhibit 10.11 to the Company's Registration Statement on Form S-1, as amended (File No. 333-264335)).
21.1***	Subsidiaries of Registrant (Incorporated by reference to Exhibit 21.1 to the Company's Registration Statement on Form S-1, as amended (File No. 333-264335)).
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.
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

* Filed herewith.

** Furnished herewith.

*** Previously filed.

† Portions of this exhibit (indicated by asterisks) will be omitted in accordance with the rules of the Securities and Exchange Commission.

Item 16. Form 10-K Summary.

None.

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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, 2022 and 2021, the related consolidated statements of operations, comprehensive loss, convertible preferred stock and stockholders' equity (deficit), and cash flows for each of the years in the two-year period ended December 31, 2022, 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, 2022 and 2021, and the results of its operations and its cash flows for each of the years in the two-year period ended December 31, 2022, 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. 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.

We have served as the Company's auditor since 2021.

/s/ KPMG LLP
Phoenix, Arizona
March 23, 2023

PEPGEN INC.
CONSOLIDATED BALANCE SHEETS
(IN THOUSANDS, EXCEPT SHARE AND PAR VALUE AMOUNTS)

	December 31,	
	2022	2021
Assets		
Current assets:		
Cash and cash equivalents	\$ 181,752	\$ 132,895
Other receivables	58	4,744
Prepaid expenses and other current assets	4,273	2,347
Total current assets	<u>\$ 186,083</u>	<u>139,986</u>
Property and equipment, net	3,335	636
Operating lease right-of-use asset	26,549	—
Other assets	1,473	3,019
Total assets	<u>\$ 217,440</u>	<u>\$ 143,641</u>
Liabilities, convertible preferred stock, and stockholders' equity (deficit)		
Current liabilities:		
Accounts payable	\$ 1,362	\$ 3,240
Accrued expenses	11,913	7,081
Operating lease liability	5,553	—
Total current liabilities	18,828	10,321
Preferred stock warrant liability	—	226
Operating lease liability, net of current portion	18,981	—
Total liabilities	<u>37,809</u>	<u>10,547</u>
Commitments and contingencies (Note 8)		
Convertible preferred stock:		
Series A-1 convertible preferred stock, \$0.0001 par value; zero and 1,372,970 shares authorized, issued, and outstanding as of December 31, 2022 and 2021, respectively; zero and \$6.4 million liquidation preference as of December 31, 2022 and 2021	—	8,454
Series A-2 convertible preferred stock, \$0.0001 par value; zero and 3,974,598 shares authorized as of December 31, 2022 and 2021; zero and 3,939,069 shares issued and outstanding as of December 31, 2022 and 2021, respectively; zero and \$45.0 million liquidation preference as of December 31, 2022 and 2021, respectively	—	44,639
Series B convertible preferred stock, \$0.0001 par value; zero and 7,234,766 shares authorized as of December 31, 2022 and 2021, respectively; zero and 7,234,766 shares issued and outstanding as of December 31, 2022 and 2021, respectively; zero and \$112.5 million liquidation preference as of December 31, 2022 and 2021, respectively	—	112,083
Stockholders' equity (deficit):		
Preferred stock, \$0.0001 par value; 10,000,000 and zero shares authorized at December 31, 2022 and 2021, respectively	—	—
Common stock, \$0.0001 par value; 500,000,000 and 16,000,000 shares authorized as of December 31, 2022 and 2021, respectively; 23,713,196 and 963,588 shares issued and outstanding as of December 31, 2022 and 2021, respectively	2	—
Additional paid-in capital	282,566	1,653
Accumulated other comprehensive income (loss)	(81)	17
Accumulated deficit	(102,856)	(33,752)
Total stockholders' equity (deficit)	<u>179,631</u>	<u>(32,082)</u>
Total liabilities, convertible preferred stock, and stockholders' equity (deficit)	<u>\$ 217,440</u>	<u>\$ 143,641</u>

See accompanying notes to consolidated financial statements.

PEPGEN INC.
CONSOLIDATED STATEMENTS OF OPERATIONS
(IN THOUSANDS, EXCEPT SHARE AND PER SHARE AMOUNTS)

	Year Ended December 31,	
	2022	2021
Operating expenses:		
Research and development	\$ 54,077	\$ 18,999
General and administrative	14,224	8,110
Total operating expenses	\$ 68,301	\$ 27,109
Operating loss	\$ (68,301)	\$ (27,109)
Other income (expense)		
Interest income	2,793	—
Other income (expense), net	110	(172)
Total other income (expense), net	2,903	(172)
Net loss before income tax	\$ (65,398)	\$ (27,281)
Income tax expense	(3,706)	—
Net loss	\$ (69,104)	\$ (27,281)
Net loss per share, basic and diluted	\$ (4.42)	\$ (30.27)
Weighted-average common shares outstanding, basic and diluted	15,639,728	901,108

See accompanying notes to consolidated financial statements.

PEPGEN INC.
CONSOLIDATED STATEMENTS OF COMPREHENSIVE LOSS
(IN THOUSANDS)

	Year Ended December 31,	
	2022	2021
Net loss	\$ (69,104)	\$ (27,281)
Cumulative translation adjustment arising during the period	(98)	25
Comprehensive loss	<u>\$ (69,202)</u>	<u>\$ (27,256)</u>

See accompanying notes to consolidated financial statements.

PEPGEN INC.
CONSOLIDATED STATEMENTS OF CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT)
(IN THOUSANDS, EXCEPT SHARE AMOUNTS)

	Series A-1 Convertible Preferred Stock	Series A-2 Convertible Preferred Stock	Series B Convertible Preferred Stock	Common Stock	Additional Paid-in Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Stockholders' Equity (Deficit)
	Shares	Shares	Shares	Shares	Amount	Amount	Amount	Amount
Balance as of December 31, 2020	1,372,970	700,278	—	894,060	119	(8)	(6,471)	(6,360)
Release of common stock from vesting restrictions	—	—	—	69,528	—	—	—	—
Issuance of Series A-2 convertible preferred stock, net of issuance cost of \$40	—	3,238,791	—	—	—	—	—	—
Issuance of Series B convertible preferred stock, net of issuance cost of \$417	—	—	7,234,766	—	—	—	—	—
Stock-based compensation expense	—	—	—	—	1,534	—	(27,281)	1,534
Net loss	—	—	—	—	—	—	—	(27,281)
Foreign currency translation adjustment	—	—	—	—	—	25	—	25
Balance as of December 31, 2021	1,372,970	3,939,069	7,234,766	963,588	\$ 1,653	\$ 17	\$ (33,752)	\$ (32,082)
Issuance of Series A-2 stock upon exercise of warrants	—	35,529	—	—	—	—	—	—
Conversion of convertible preferred stock upon IPO	(1,372,970)	(3,974,598)	(7,234,766)	12,359,856	1	—	—	165,752
Issuance of common stock in IPO, net of underwriters' fees and issuance costs of \$12,684	—	—	—	10,238,951	1	—	—	110,183
Release of common stock from vesting restrictions	—	—	—	69,529	—	—	—	—
Exercise of stock options	—	—	—	81,272	217	—	—	217
Stock-based compensation expense	—	—	—	—	4,763	—	—	4,763
Net loss	—	—	—	—	—	—	(69,104)	(69,104)
Foreign currency translation adjustment	—	—	—	—	—	(98)	—	(98)
Balance as of December 31, 2022	—	—	—	23,713,196	2	(81)	(102,856)	179,631

See accompanying notes to consolidated financial statements.

PEPGEN INC.
CONSOLIDATED STATEMENTS OF CASH FLOWS
(IN THOUSANDS)

	Year Ended December 31,	
	2022	2021
Cash flows from operating activities:		
Net loss	\$ (69,104)	\$ (27,281)
Adjustments to reconcile net loss to cash used in operating activities:		
Depreciation	493	178
Stock-based compensation expense	4,763	1,534
Change in fair value of preferred stock warrant liability	(58)	196
Other non-cash adjustments	134	—
Changes in operating assets and liabilities:		
Other receivables	4,183	(4,342)
Operating lease, right-of-use asset	—	—
Prepays and other current and non-current assets	(1,784)	(2,215)
Accounts payable	(1,407)	2,510
Accrued expenses and other non-current liabilities	5,531	6,821
Operating lease liabilities, current and non-current	(2,016)	—
Net cash used in operating activities	(59,265)	(22,599)
Cash flows from investing activities:		
Purchases of property and equipment	(3,755)	(500)
Net cash used in investing activities	(3,755)	(500)
Cash flows from financing activities:		
Issuance of common stock upon initial public offering, net of underwriters' fees	114,267	—
Payment of offering costs	(2,697)	(1,386)
Proceeds from issuance of common stock upon exercise of Series A-2 warrants	406	—
Proceeds from issuance of Series A-2 convertible preferred stock, net of issuance costs	—	36,959
Proceeds from issuance of Series B convertible preferred stock, net of issuance costs	—	112,083
Proceeds from exercise of stock options	217	—
Net cash provided by financing activities	112,193	147,656
Effect of exchange rate changes on cash	(316)	33
Net increase in cash, cash equivalents and restricted cash	\$ 48,857	\$ 124,590
Cash, cash equivalents and restricted cash at beginning of period	134,368	9,778
Cash, cash equivalents and restricted cash at end of period	\$ 183,225	\$ 134,368
Components of cash, cash equivalents and restricted cash		
Cash and cash equivalents	\$ 181,752	\$ 132,895
Restricted cash	1,473	1,473
Total cash, cash equivalents and restricted cash at end of period	\$ 183,225	\$ 134,368
Supplemental noncash investing and financing activities		
Property and equipment included in accounts payable and accrued expenses	\$ 363	\$ —
Lease assets obtained in exchange for new operating lease liabilities	26,549	—
Deferred offering costs included in accounts payable and accrued expenses	—	160

See accompanying notes to consolidated financial statements.

PEPGEN INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

1. Nature of Business and Basis of Presentation

PepGen Inc. (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 UK. On November 9, 2020, PepGen Limited completed 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 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 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 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 Inc. as the Reorganization was deemed to be between entities under common control.

Initial Public Offering

On May 10, 2022, the Company closed its initial public offering (IPO) in which the Company 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, the Company 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 the Company issued 1,238,951 shares of common stock for gross proceeds of \$14.9 million. From the IPO and option exercise by the underwriters, the Company received approximately \$122.9 million in gross proceeds and \$110.2 million in net proceeds, after deducting underwriting discounts and estimated offering expenses payable by the Company.

Immediately prior to consummation of the IPO, all 12,546,805 outstanding shares of the Company's redeemable convertible preferred stock, and 35,529 preferred stock warrants that were exercised on May 4, 2022 (see Note 3), converted into 12,359,856 shares of the Company's common stock. As a result of this conversion, the Company's net loss per share, basic and diluted, will be significantly different in future filings.

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 and cash equivalents to date have been to fund 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, 2022, the Company had an accumulated deficit of \$102.9 million. To date, the Company has funded operations primarily through private placements of convertible preferred stock and its IPO. As of December 31, 2022, the Company had cash and cash equivalents of \$181.8 million. Based on its current operating plans, the Company believes that its cash and cash equivalents as of December 31, 2022, will be sufficient to fund its currently planned operations for at least the next 12 months from the filing of these consolidated financial statements.

As the Company continues to pursue its business plan to successfully develop and obtain regulatory approval for the Company's 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 UK corporation) and PepGen Securities Corp. All intercompany accounts and transactions have been eliminated in consolidation.

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 the 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. As the Company operates as one operating segment, all required segment financial information is presented in the consolidated financial statements.

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 foreign currency translation adjustment, a component of accumulated other comprehensive loss in stockholders' deficit.

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, 2022, the Company's cash and money market accounts were held by one financial institution in the U.S. and one financial institution in the U.K. At times, the Company's deposits held in the U.S. and U.K. may exceed the Federal Depository Insurance Corporation and Financial Services Compensation Scheme, respectively, insured limits.

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, 2021, deferred offering costs of \$1.5 million were recorded within other assets on the consolidated balance sheets. Subsequent to the completion of the IPO in May 2022, deferred offering costs totaling \$4.1 million were recorded within stockholders' equity as a reduction of additional paid-in-capital generated from the initial public offering.

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.

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, 2022 and 2021, cash and cash equivalents consisted primarily of checking and money market funds composed of US government obligations.

Restricted Cash

The Company classifies all cash whose use 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. As of December 31, 2022 and 2021, \$1.5 million of restricted cash was recorded in other assets on the consolidated balance sheets.

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

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, 2022 and 2021.

Leases

Effective January 1, 2022, the Company adopted ASU 2016-02, Leases (Topic 842) (“ASC 842”). Under 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 assets 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 incremental borrowing rate, the Company used 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 a 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.

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, 2022 and 2021 that were material to the consolidated financial statements.

Convertible Preferred Stock

The Company recorded convertible preferred stock at fair value on the dates of issuance, net of issuance costs. Upon the occurrence of certain events that are outside the Company's control, including a deemed liquidation event, holders of the convertible preferred stock can cause redemption for cash. Therefore, convertible preferred stock was classified outside of stockholders' deficit on the consolidated balance sheets as events triggering the liquidation preferences are not solely within the Company's control. No accretion was recognized as the contingent events that could give rise to redemption were not deemed probable. Upon completion of the IPO, all preferred stock was converted to common stock and as such no amounts were issued or outstanding as of December 31, 2022.

Preferred Stock Warrants

The Company classified warrants to purchase its Series A-2 convertible preferred stock as a liability on the consolidated balance sheets as these warrants were freestanding financial instruments that could require the Company to transfer assets upon exercise.

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 recognizes the benefit of government grants and refundable research and development tax credits as a reduction of research and development expense when it is probable that the Company has complied with the conditions attached and will receive reimbursement. Government grants and refundable research and development tax credits are included in other receivables within the consolidated balance sheets. For the years ended December 31, 2022 and 2021, the Company recorded nil and \$4.8 million as reductions of research and development expense in the consolidated statements of operations, respectively. During the year-ended December 31, 2022, the Company received £3.4 million (approximately \$4.1 million) relating to its 2021 United Kingdom research and development tax credit for research and development activities undertaken by its U.K. subsidiary. As of December 31, 2022 and 2021, nil and \$4.7 million of research and development tax credits were recorded in other receivables on the consolidated balance sheets, respectively.

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.

Common Stock Valuation

Prior to the Company's IPO, due to the absence of an active market for the Company's common stock, the Company utilized methodologies, approaches and assumptions consistent with the American Institute of Certified Public Accountants' Audit and Accounting Practice Guide: Valuation of Privately-Held Company Equity Securities Issued as Compensation to estimate the fair value of its common stock. In determining the exercise prices for options granted, the Company has considered the fair value of the common stock as of the grant date. The fair value of the common stock has been determined based upon a variety of factors, including valuations of the Company's common stock performed with the assistance of independent third-party valuation specialists; the Company's stage of development and business strategy, including the status of research and development efforts of its product candidates, and the material risks related to its business and industry; the Company's business conditions and projections; the Company's results of operations and financial position, including its levels of available capital resources; the valuation of publicly traded companies in the life sciences and biotechnology sectors, as well as recently completed mergers and acquisitions of peer companies; the lack of marketability of the Company's common stock as a private company; the prices of the Company's convertible preferred stock sold to investors in arm's length transactions and the rights, preferences and privileges of its convertible preferred stock relative to those of its common stock; the likelihood of achieving a liquidity event for the holders of the Company's common stock, such as an initial public offering or a sale of the Company given prevailing market conditions; trends and developments in its industry; the hiring of key personnel and the experience of management; and external market conditions affecting the life sciences and biotechnology industry sectors. Significant changes to the key assumptions underlying the factors used could result in different fair values of common stock at each valuation date.

Stock-Based Compensation

The Company accounts for its stock-based compensation in accordance with ASC Topic 718, *Compensation-Stock Compensation* (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 options granted using the Black-Scholes option pricing model (Black-Scholes) for stock option grants to both employees and non-employees. 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, directors and non-employees 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 a 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 options granted to employees and non-employees whereby, the expected term equals the arithmetic average of the vesting term and the original contractual term of the 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.

Prior to the Company's IPO, there was no public market for its common stock, and consequently, the estimated fair value of its common stock was determined by the board of directors as of the date of each option grant, with input from management, considering third-party valuations of its common stock as well as its 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* (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 the Company's common stock at each valuation date.

Subsequent to the Company's IPO, the fair value of the common stock underlying the 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.

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, which include convertible preferred stock and unvested common stock under the Company's equity incentive plan, vesting conditions placed on previously issued common shares and warrants to purchase convertible preferred stock 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,	
	2022	2021
Series A-1 convertible preferred stock	—	1,372,970
Series A-2 convertible preferred stock	—	3,939,069
Series A-2 convertible preferred stock warrants	—	35,529
Series B convertible preferred stock	—	7,234,766
Options to purchase common stock	3,341,834	1,898,084
Vesting conditions placed on previously issued common shares	—	69,528
Total	<u>3,341,834</u>	<u>14,549,946</u>

Emerging Growth Company Status

The Company is an "emerging growth company," as defined in the Jumpstart Our Business Startups Act, 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 an offering 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 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 of 2012 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 February 2016, the FASB issued ASU 2016-02, Leases (Topic 842), the amendment relates to leases to increase transparency and comparability among organizations by requiring the recognition of right-of-use, or the ROU, assets obtained in exchange for lease liabilities on the balance sheet. Most prominent among the changes in the standard is the recognition of ROU assets and lease liabilities by lessees for those leases classified as operating leases. Under the standard, disclosures are required to meet the objective of enabling users of consolidated financial statements to assess the amount, timing, and uncertainty of cash flows arising from leases. The effective date of this update is for fiscal years beginning after December 15, 2021, and interim periods therein. The Company adopted the standard on January 1, 2022. On December 29, 2022, the Company commenced a lease for accounting purposes, resulting in the recording of a lease liability and corresponding right of use asset on the consolidated balance sheet in accordance with Topic 842 (refer to Note 6). Prior to commencing this lease in December 2022, the Company had no leases with initial terms greater than 12 months and had no right-of-use assets or lease liabilities.

In June 2016, the FASB issued ASU 2016-13, Financial Instruments—Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments. The standard changes how entities will measure credit losses for most financial assets, including accounts and notes receivables. The standard will replace today’s “incurred loss” approach with an “expected loss” model, under which companies will recognize allowances based on expected rather than incurred losses. Entities will apply the standard’s provisions as a cumulative-effect adjustment to retained earnings as of the beginning of the first reporting period in which the guidance is effective. The effective date of this update is for fiscal years beginning after December 15, 2022, and interim periods therein. The Company is currently assessing the impact of adopting this standard on the Company’s consolidated financial statements and related disclosures.

In November 2019, the FASB issued ASU 2019-11, Codification Improvements to Topic 326, Financial Instruments—Credit Losses. The standard is an accounting pronouncement that amends ASU 2016-13, “Financial Instruments – Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments.” The amendments update guidance on reporting credit losses for financial assets. These amendments affect loans, debt securities, trade receivables, net investments in leases, off balance sheet credit exposures, reinsurance receivables, and any other financial assets not excluded from the scope that have the contractual right to receive cash. The amendments in both ASU 2016-13 and ASU 2019-11 are effective for annual reporting periods beginning after December 15, 2019, including interim periods within those fiscal years. The Company does not expect ASU 2016-13 and ASU 2019-11 to have a material impact on its consolidated financial statements and financial statement disclosures.

In December 2019, the FASB issued ASU 2019-12, Income Taxes (Topic 740). The standard simplifies the Accounting for Income Taxes. The standard simplifies the accounting for income taxes by removing certain exceptions to the general principles in Topic 740 and also improves consistent application by clarifying and amending existing guidance. The standard is effective for fiscal years beginning after December 15, 2021, and interim periods within fiscal years beginning after December 15, 2022. The Company is assessing the impact of this guidance and is continuing to evaluate the impact on its consolidated financial statements.

3. Fair Value Measurements

The following table set forth the fair value of the Company’s financial assets measure at fair value on a recurring basis and indicates the level within the fair value hierarchy utilized to determine such values (in thousands):

	As of December 31, 2022			
	Total	Level 1	Level 2	Level 3
US Treasury-backed money market funds	\$ 18,645	\$ 18,645	—	—
Total	\$ 18,645	\$ 18,645	\$ —	\$ —

	As of December 31, 2021			
	Total	Level 1	Level 2	Level 3
US Treasury-backed money market funds	\$ 30,719	\$ 30,719	—	—
Total	\$ 30,719	\$ 30,719	\$ —	\$ —

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 balance sheet under cash and cash equivalents.

Preferred stock warrant liability

In connection with the November 24, 2020 Stock Purchase Agreement (Note 8), the Company granted warrants to purchase up to 35,529 shares of Series A-2 convertible preferred stock at a price per share equal to \$11.42 and with a term ending upon the earlier of an underwritten public offering pursuant to an effective registration statement under the Securities Act of 1933, the consummation of a Deemed Liquidation Event, as such term is defined in the Company's Restated Certificate of Incorporation or 10 years. As the warrants are for preferred stock, which do not qualify for equity classification, the warrants were recorded as a liability and were required to be remeasured to fair value at each reporting date. The warrants were exercised on May 4, 2022, just prior to the completion of the IPO, for proceeds of \$0.4 million. Immediately prior to the consummation of the IPO, the warrants were converted into 34,901 shares of the Company's common stock.

As there are a number of inputs that are not observable in the market, the warrant valuation represented a Level 3 measurement within the fair value hierarchy. The Company's valuation of the preferred stock warrant utilized the Black-Scholes option-pricing model, which incorporates assumptions and estimates to value the preferred stock warrant.

The quantitative elements associated with the Company's Level 3 inputs impacting the fair value measurement of the preferred stock warrant liability included the fair value per share of the underlying Series A-2 convertible preferred stock, the remaining contractual term of the warrant, risk-free interest rate, expected dividend yield and expected volatility of the price of the underlying preferred stock. The most significant assumption in the Black-Scholes option-pricing model impacting the fair value of the preferred stock warrant was the fair value of the Company's Series A-2 convertible preferred stock as of each remeasurement date. The Company determined the fair value per share of the underlying preferred stock by taking into consideration its most recent sales of its convertible preferred stock. The Company historically had been a private company and lacked company-specific historical and implied volatility information of its stock. Therefore, it estimated its expected stock volatility based on the historical volatility of publicly traded peer companies for a term equal to the remaining contractual term of the warrant. The risk-free interest rate was determined by reference to the U.S. Treasury yield curve for time periods approximately equal to the remaining contractual term of the warrant. The Company had estimated a 0% dividend yield based on the expected dividend yield and the fact that the Company has never paid or declared dividends.

The Company recognized changes in the fair value of the warrant liability as a component of other income (expense) in its consolidated statements of operations and comprehensive loss.

A reconciliation of the Level 3 warrant liability through exercise in the second quarter of 2022 is as follows (in thousands):

	Series A-2 Preferred Stock Warrant Liability
Balance as of December 31, 2020	\$ 30
Change in fair value	196
Balance as of December 31, 2021	226
Change in fair value	(58)
Exercise of preferred stock warrants	(168)
Balance as of December 31, 2022	\$ 0

4. Property and Equipment, Net

The cost and accumulated depreciation of property and equipment were as follows (in thousands):

	December 31,	
	2022	2021
Lab equipment	\$ 2,424	\$ 975
Computer and office equipment	171	91
Construction in process	1,129	—
Total property and equipment	3,724	1,066
Less accumulated depreciation	(389)	(430)
Total property and equipment, net	\$ 3,335	\$ 636

Depreciation expense was \$0.5 million and \$0.2 million for the year ended December 31, 2022 and 2021, respectively.

5. Accrued Expenses

Accrued expenses consisted of the following (in thousands):

	December 31,	
	2022	2021
Research and development	\$ 4,840	\$ 5,343
Employee-related expenses	2,440	1,205
Taxes payable	3,248	—
Other	1,385	533
Total accrued expenses	\$ 11,913	\$ 7,081

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 begins in March 2023, and will be \$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. Due to the timing of the lease commencement date at the end of 2022, there was no fixed lease rent expense associated with the Harrison Lease in 2022. At December 31, 2022, the Harrison Lease was the only lease for which the Company recorded a lease liability and corresponding right-of-use asset.

The landlord is completing significant leasehold improvements to the leased space, a portion of which the Company is obligated to pay per the term of the Harrison Lease. The Company paid \$2.0 million for the improvements prior to lease commencement, and expects to pay approximately \$3.9 million for the improvements in 2023. The Company has determined that the landlord is the accounting owner of the improvements, and expected payments by the Company for the improvements have been included in the calculation of the right-of-use asset and lease liability.

During 2022, 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, on an initial lease term from February 1, 2022 to January 31, 2023, which the Company extended until March 2023. The Company also leased space at Innovation Building, University

of Oxford in Oxford, United Kingdom. The Company terminated its lease in Oxford in July 2022. All of these leases had 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, 2022	December 31, 2021
Fixed lease cost	\$ —	\$ —
Short-term lease cost	1,294	520
Total lease cost	<u>\$ 1,294</u>	<u>\$ 520</u>

The Company recorded immaterial variable lease costs for the years ended December 31, 2022 and 2021.

Supplemental disclosure of cash flow information under ASC 842 for the leases were as follows (in thousands):

	December 31, 2022
Operating cash payments for operating leases	<u>\$ 2,016</u>

Cash payments for operating leases during 2022 related to tenant improvements made to the office and lab space prior to the Company obtaining occupancy. These payments were recorded in the right-of-use asset at December 31, 2022.

The remaining lease term for the Harrison Lease is 9.2 years, and the discount rate is 8.0%.

Future minimum lease payments under the non-cancelable operating leases consisted of the following as of December 31, 2022:

Year Ending December 31,	(in thousands)
2023	\$ 6,289
2024	3,033
2025	3,124
2026	3,218
2027	3,315
Thereafter	14,906
Total future minimum lease payments	\$ 33,885
Less: imputed interest	(9,351)
Present value of lease liability	<u>\$ 24,534</u>
Included in the consolidated balance sheet (in thousands)	December 31, 2022
Lease liability	\$ 5,553
Lease liability, net of current portion	18,981
Total lease liability	<u>\$ 24,534</u>

7. Related Party Transactions

Technology license agreement

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, or the License Agreement, which was subsequently amended in December 2018 and further amended and restated in November 2020. The Licensors and affiliates hold 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 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 of \$0.1 million upon transfer of the license technology and data and in 2020 upon amending and restating the License Agreement made two additional payments of \$19,000 for a Restatement Completion Fee and License Data Fee. The Company determined that the upfront payment and subsequent

Restatement Completion Fee and License Data Fee as part of the license agreement would be expensed upon execution of the original contract and subsequent amendment as the license was acquired for research and development purposes which does not have alternative future uses, and the underlying technology has not reached technological feasibility.

The Company could be required to make milestone payments to the Licensors upon completion 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. 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 or sublicensees in excess of a threshold amount between £20 million and £30 million (\$24.2 million and \$36.3 million as of December 31, 2022), 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 agreement.

Upon completion of the Company's Initial Public Offering, or IPO in May 2022, 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 IPO raise, was \$1.4 million, which was paid during the second quarter of 2022 and included in research and development expense on the consolidated statement of operations.

Additionally, the Company paid office space rent to OUI. For the years ended December 31, 2022 and 2021, total rent payments were \$0.2 million and \$0.2 million, respectively. As of December 31, 2022 and 2021, nil and \$30,000, respectively, was due to OUI by the Company.

Services agreement

In November 2020, the Company entered into an agreement, or the Services Agreement, with Carnot Pharma, LLC, or Carnot, under which Carnot provides research and other services to the Company. Carnot is an entity controlled by RA Capital Management, L.P. Entities affiliated with RA Capital Management, L.P. purchased shares of Series A-2 convertible preferred stock in the Company's preferred stock financing in November of 2020 and May and July of 2021. In addition, entities affiliated with RA Capital Management, L.P. purchased shares of our Series B convertible preferred stock in the Company's preferred stock financing in July 2021. Two members of the Company's Board of Directors are also affiliated with RA Capital Management, L.P.

Under the terms of the Services Agreement, the Company compensates Carnot on a fully burdened cost basis for personal time devoted to Company projects. In addition, the Company reimburses Carnot on a costs basis for any subcontractor costs incurred. The Company pays Carnot on a quarterly basis, in arrears, for services performed and costs incurred. The Services Agreement is for a term of the later of (A) two (2) years and (B) the later of (a) completion of the Services or (b) latest-to-occur delivery of a final report or any other items required to be delivered to the Company under the last ongoing project as part of the services, if any. The Company may terminate the services agreement by giving 30 days' prior notice and either party can terminate the services agreement for a material breach, if not cured within 30 days following notice by the non-breaching party. The services agreement was terminated on April 15, 2022.

Expenses incurred by the Company under the Services Agreement with Carnot for the year ended December 31, 2022 and 2021, totaled \$0.1 million and \$0.8 million, respectively. As of December 31, 2022 and 2021, nil and \$2,600 was due to Carnot by the Company for services rendered under the Services Agreement, respectively.

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, 2022. 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. Convertible Preferred Stock and Stockholders' Equity

Reverse Stock Split

On April 29, 2022, the Company filed a charter amendment to affect a 1.018 for 1 reverse stock split of its issued and outstanding shares of common stock, which resulted in a proportional adjustment to the existing conversion ratios for each series of the Company's preferred stock. Accordingly, all share and per share amounts for all periods presented in the accompanying consolidated financial statements and notes thereto have been adjusted retroactively, where applicable, to reflect this reverse stock split and adjustment of the preferred stock conversion ratios.

Series A-1 convertible preferred stock and Series A-2 convertible preferred stock

In connection with the November 24, 2020, Stock Purchase Agreement, the Company agreed to issue an aggregate of 3,939,069 shares of Series A-2 convertible preferred stock to new and existing investors at a price of \$11.42 per share, in three closings, and elected to convert 1,348,693 shares of outstanding Class A and Class B common stock into 1,372,970 shares of Series A-1 convertible preferred stock. A total of 1,033,117 shares of Class A common stock held by certain founding investors and employees were not modified and continue to exist as Class A common stock. The Series A-1 and Series A-2 convertible preferred stock was converted to common stock immediately prior to the consummation of the Company's IPO in May 2022 (see Note 1).

Series B convertible preferred stock

In July 2021 the Company entered into the Series B Stock Purchase Agreement, whereby the Company agreed to issue and sold an aggregate of 7,234,766 shares of Series B convertible stock to new and existing investors at a per share price of \$15.55 per share for aggregate gross proceeds of \$112.5 million. The Series B convertible preferred stock was converted to common stock immediately prior to the consummation of the Company's IPO in May 2022 (see Note 1).

Common stock

Under the Third Amended and Restated Certificate of Incorporation, dated May 10, 2022, 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). In connection with the IPO, the Company re-designated all shares of Class A common stock as shares of common stock. 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 have been declared by the board of directors during the year ended December 31, 2022 and December 31, 2021.

The Company has reserved the following shares of common stock for issuance, on an as-converted basis for 2021, as follows:

	December 31,	
	2022	2021
Convertible preferred stock	—	12,546,805
Stock options issued and outstanding	3,341,834	1,898,084
Preferred stock warrants issued and outstanding	—	35,529
Vesting conditions placed on previously issued common shares	—	69,529
Authorized for future stock awards or option grants	901,462	456,416
Authorized for future issuance under employee stock purchase plan	226,000	—
Total	4,469,296	15,006,363

Shares of Common Stock Subject to Repurchase

In November 2020, in connection with the Series A-2 convertible preferred stock financing, two founding stockholders entered into Stock Restriction Agreements, or Restriction Agreements, whereby 139,057 shares that were previously vested and not subject to repurchase became restricted and subject to repurchase. The repurchase rights lapse 50% on the one-year anniversary of the Restriction Agreements and 50% on the second anniversary of the Restriction Agreements. Shares subject to repurchase by the

Company are not deemed, for accounting purposes, to be outstanding until those shares vest and therefore are not included in the shares outstanding on the consolidated balance sheet.

In connection with the vesting restrictions placed on these previously vested shares, the Company was required to determine the measurement date fair value of the shares, which was \$2.37 per share or \$0.3 million in aggregate. The measurement date fair value of the restricted stock will be recognized as stock-based compensation expense over the vesting period. As of December 31, 2022 and 2021, zero and 69,529 shares were subject to repurchase by the Company, respectively.

10. Stock-Based Compensation

The Company maintains three equity compensation plans; the 2020 Stock Plan, or the 2020 Plan, the 2022 Stock Option Incentive Plan, or the 2022 Plan, and the 2022 Employee Stock Purchase Plan, or the ESPP. The number of shares of common stock that may be issued under the 2022 Plan is subject to increase by the number of shares forfeited under any 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 board of directors has determined not to make any further awards under the 2020 plan. As of December 31, 2022, 901,462 shares remained available for grant under the 2022 Plan and 226,000 shares remained available for grant under the ESPP.

Stock Option Valuation

In determining the fair value of the stock options granted, the Company uses the Black-Scholes option-pricing model and 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 was estimated based the average historical volatilities for comparable publicly traded pharmaceutical 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. The Company expects to estimate stock volatility based on the historical volatility of peer companies until such time as it has adequate historical data regarding the volatility of its own traded stock price.

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,	
	2022	2021
Risk-free interest rate %	2.95%	1.10%
Expected volatility %	71.68%	77.00%
Expected term (in years)	6.08	6.03
Expected dividend yield	—	—

Stock Option Activity

Stock option activity under the Plan, is 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, 2021	1,898,084	\$ 7.46	9.6	\$ 7,157
Granted	1,544,285	11.69		
Exercised	(81,272)	2.71		
Canceled/Forfeited	(19,263)	9.51		
Outstanding as of December 31, 2022	3,341,834	\$ 9.52	8.7	\$ 12,877
Vested and exercisable as of December 31, 2022	681,880	\$ 6.38	8.2	\$ 4,764
Vested and expected to vest as of December 31, 2022	3,341,834	\$ 9.52	8.7	\$ 12,877

The aggregate intrinsic value of options is calculated as the difference between the exercises price of the options and the fair value of the Company's common stock for those options that had exercises prices lower than the fair value of the Company's common stock. The total intrinsic value of the options exercised during the year ended December 31, 2022 and 2021 was \$0.9 million and nil, 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, 2022 and 2021, the total proceeds to the Company from stock option exercises was \$0.2 million and nil, respectively.

The weighted-average grant date fair value of options granted during the year ended December 31, 2022 and 2021 was \$7.66 and \$5.22 per share, respectively.

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,	
	2022	2021
Research and development	\$ 1,695	\$ 394
General and administrative	3,068	1,140
Total stock-based compensation expense	\$ 4,763	\$ 1,534

The Company had 3,341,834 unvested options outstanding as of December 31, 2022. As of December 31, 2022, total unrecognized compensation cost related to stock options was \$15.8 million. This amount is expected to be recognized over a weighted average period of approximately 2.98 years.

11. Income Taxes

The Company's loss before income taxes for the years ended December 31, 2022 and 2021 were generated in the following jurisdictions (in thousands):

	Year Ended December 31,	
	2022	2021
Domestic	\$ (96,781)	\$ (6,181)
Foreign	31,383	(21,100)
Worldwide	\$ (65,398)	\$ (27,281)

The foreign income for the year-ended December 31, 2022 was due to the transfer of intellectual property (IP) from PepGen Limited to the parent company, PepGen Inc., in an arm's length transaction at fair value pursuant to an asset transfer agreement.

The components of net deferred income taxes consisted of the following as of December 31, 2022 and 2021 (in thousands):

	December 31,	
	2022	2021
Deferred tax assets:		
Net operating loss carryforwards	\$ 474	\$ 3,103
Research and development credits	1,287	36
Accrued expenses	523	234
Capitalized Section 174 R&D Costs	11,818	—
Stock compensation accruals	1,081	264
Right-of-use liability	5,760	—
Intangible asset amortization	6,879	—
Deferred tax assets	<u>27,822</u>	<u>3,637</u>
Deferred tax liabilities		
Right-of-use-Asset	(6,233)	
Fixed Assets	(45)	(13)
Other, net	(2)	—
Deferred tax liabilities	<u>(6,280)</u>	<u>(13)</u>
Net deferred tax assets	21,542	3,624
Valuation allowance	(21,542)	(3,624)
Net deferred tax assets	<u>\$ —</u>	<u>\$ —</u>

The components of income tax expense were as follows for the years ended December 31, 2022 and 2021 (in thousands):

	Year Ended December 31,	
	2022	2021
Current expense:		
U.S. Federal	\$ —	\$ —
State	23	—
Foreign	3,683	—
Total current expense	<u>3,706</u>	<u>—</u>
Deferred expense:		
U.S. Federal	—	—
State	—	—
Foreign	—	—
Total deferred expense	<u>—</u>	<u>—</u>
Provision for income taxes	<u>\$ 3,706</u>	<u>\$ —</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, 2022 and 2021, as follows:

	Year Ended December 31,	
	2022	2021
Tax at statutory rate	21.0%	21.0%
State tax (net of federal benefit)	(0.0)%	0.7%
Permanent differences	(0.1)%	(0.6)%
Research and development credit	1.6%	0.2%
GILTI Inclusion	(8.8)%	—
UK R&D credit	0.0%	(9.4)%
Foreign rate differential	(1.0)%	(1.5)%
Change in valuation allowance	(23.4)%	(10.3)%
Other	5.0%	(0.1)%
Income tax expense (benefit)	<u>(5.7)%</u>	<u>—</u>

The Company's income tax expense of \$3.7 million for the year ended December 31, 2022, compared to nil for the year ended December 31, 2021. The income tax expense for the year ended December 31, 2022 was due to the intellectual property (IP) transfer noted in the paragraph below.

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 Inc., in an arm's length transaction at fair value pursuant to an asset transfer agreement. The fair value of the IP assets is a non-recurring fair value measurement. The Company engaged valuation specialists to calculate the IP value, and the IP value was measured using the historical cost method. The historical cost method estimated the fair value of the IP assets using the historical cost base of the IP assets and the expected market return as of the Transfer Date. The significant assumption inherent in estimating the fair value using the historical cost method was the expected market return. The Company utilized a 40% expected market return, which a third-party investor may expect as a return on their investment, and which is based on studies of venture capital investment returns. The Company calculated the fair value of the IP assets by computing the present value of the historical cost base using the 40% expected market return. The expected market return assumption used in the estimation of the IP assets represents a Level 3 input of the fair value hierarchy (see Note 3).

The Company had federal research and development (R&D) credits of approximately \$1.4 million as of December 31, 2022, before consideration of limitations under Section 382 of the Internal Revenue Code or Section 382, as further described below. The R&D credits will expire beginning in 2041. The Company has state net operating losses of \$16.3 million and state R&D credits of \$0.3 million which begin expiring in 2042.

The future utilization of the Company's state NOL's and federal and state R&D credits to offset future taxable income may be subject to a substantial annual limitation as a result of changes in ownership by stockholders that hold 5% or more of the Company's common stock. An assessment of such ownership changes under Section 382 was not completed through December 31, 2022. 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.

The Company is subject to taxation in the U.S. and the UK. The Company's federal and state returns since inception are subject to examination due to the carryover of net operating losses. The Company has not been, nor is it currently, under examination by any tax authorities. The UK tax returns from 2018 and forward are subject to examination by the UK tax authorities.

The following table summarizes the reconciliation of the beginning and ending amount of total unrecognized tax benefits for each of the periods indicated:

	December 31,	
	2022	2021
Balance at beginning of the period	\$ —	\$ —
Increase related to current year tax positions	751	—
Increase related to prior year tax positions	—	—
Decrease related to prior year tax positions	—	—
Currency translation	(78)	—
Balance at the end of the period	<u>\$ 673</u>	<u>\$ —</u>

The Company does not expect that the amount of unrecognized tax benefits to change significantly in the next twelve months. The Company's policy is to recognize interest and/or penalties related to income tax matters in income tax expense. It had no accrual for interest or penalties on its consolidated balance sheets at December 31, 2022 or 2021. No interest and/or penalties were recognized in 2022 or 2021.

12. Subsequent Events

On March 10, 2023, Silicon Valley Bank (SVB) was closed by the California Department of Financial Protection and Innovation, which appointed the Federal Deposit Insurance Corporation as receiver. On March 12, 2023 the Federal Deposit Insurance Corporation ("FDIC") transferred all deposits, both insured and uninsured, and substantially all assets from the former SVB to a newly created, full-service FDIC-operated "bridge bank", Silicon Valley Bridge Bank, N.A. and the FDIC, Treasury Department, and Federal Reserve announced that all deposits will be fully protected, whether or not they had been insured by the FDIC. As of the date of the filing of these consolidated financial statements with the Securities and Exchange Commission, the Company has full access to and control over all its cash and cash equivalents.



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