



DESIGN
THERAPEUTICS

2022

ANNUAL REPORT



Dear Fellow Shareholders,

Our founding scientific breakthrough showed the potential of novel small molecules to modulate expression of specific genes *without irreversible gene therapy or gene editing*. We call these small molecules gene targeted chimeras or GeneTAC™ molecules. Our GeneTAC™ molecules are designed to specifically address the root cause of inherited nucleotide repeat diseases by harnessing an individual's natural transcription machinery to dial up or dial down the expression of mutated genes. Our GeneTAC™ small molecules are designed to maximize pharmaceutical properties such as safety, distribution to affected organs, and suitability for standard administration and can be tailored and dose adjusted to help optimize therapeutic effect and tolerability.

There are more than 40 known debilitating, progressive diseases caused by inherited nucleotide repeat expansions and very few therapeutic options available. Over the past year, we have taken tremendous strides toward our goal of bringing novel treatments to people living with such diseases —*exemplified by the first clinical data from our portfolio with our lead program, DT-216*, a GeneTAC™ small molecule for the treatment of Friedreich ataxia (FA). FA is a devastating multisystem, degenerative disease caused by inherited GAA repeat expansions in the frataxin (FXN) gene that impairs transcription and reduces gene expression. Low FXN levels result in the clinical manifestations of FA, including neurological deficits such as loss of balance and coordination, cardiomyopathy and arrhythmias, diabetes and other disabling symptoms and conditions. In March 2022, we began clinical development with DT-216 in a Phase 1 single-ascending dose (SAD) study in patients with FA. In December 2022, we reported positive initial data from the SAD clinical trial showing that DT-216 was generally well-tolerated and was able to overcome the impairment of FXN transcription that causes FA, with a greater than two-fold increase in FXN mRNA expression. These data provided proof-of-mechanism for our compound in people with FA and supported the continued advancement of DT-216 in the ongoing multiple-ascending dose (MAD) Phase 1 study. We plan to report initial data from this study in mid-2023.

At the end of last year, we nominated our second GeneTAC™ development candidate, DT-168, an eye drop for the treatment of Fuchs endothelial corneal dystrophy, or FECD. FECD affects millions of people in the U.S. and is characterized by progressive corneal degeneration leading to vision loss. Approximately 75-80% of FECD cases are caused by a CTG trinucleotide repeat expansion of the transcription factor 4 (TCF4) gene, which leads to formation of pathogenic RNA foci in the nucleus and the mis-splicing of multiple transcripts. There are no disease-modifying therapies approved for FECD and advanced cases generally require ocular surgery, including corneal transplant. In preclinical studies, DT-168 led to robust reductions in the number of pathogenic nuclear RNA foci and corrected key mis-spliced transcripts in FECD corneal endothelial cells *in vitro*. Additionally, DT-168 was well tolerated after multiple doses in animal studies and distributed throughout the cornea following topical ocular administration. We are incredibly encouraged by these preclinical data and plan to submit an Investigational New Drug application (IND) in the second half of 2023, with the initiation of Phase 1 expected soon thereafter.

We have also continued to advance our program for myotonic dystrophy type 1 (DM1), a devastating progressive multisystem disease affecting skeletal muscle, heart, brain, eyes and other organs. DM1 is caused by an autosomal dominant mutation in the DMPK gene characterized by a CTG nucleotide

expansion, formation of pathogenic RNA foci in the nucleus and mis-splicing of multiple transcripts. It affects more than 70,000 individuals in the U.S. and more than 90,000 individuals in Europe. Like our FA and FECD programs, our DM1 GeneTAC™ molecules are designed to specifically address the underlying genetic cause of the disease and stand to benefit from the favorable development advantages of small molecules. Specifically, they are designed to selectively target the mutant DMPK allele and preserve expression of the normal allele, significantly reducing the number of pathogenic CUG hairpin RNA structures that trap splicing proteins. In *in vitro* experiments in DM1 cells, our DM1 GeneTAC™ molecules robustly reduced nuclear foci and reversed the mis-splicing characteristic of DM1. In *in vivo* experiments, DM1 molecules distributed readily to typically affected organs, including heart, skeletal muscle and even the CNS. We expect to complete IND-enabling studies for this program and submit an IND in 2024—***positioning us to have three programs in clinical development in the next two years.***

Beyond our first three programs, we continue to make significant progress across a number of exciting opportunities in our GeneTAC™ portfolio with potential to address other serious nucleotide repeat expansion-driven monogenic diseases.

In the sixth year since our founding, Design has begun to deliver on the promise of our GeneTAC™ platform by demonstrating proof of mechanism of FA GeneTAC™ molecules in people with FA and adding a second GeneTAC™ development candidate, an eye drop, for treatment of FECD.

Looking ahead, 2023 is poised to be another important year for Design as we expect to report initial data from the Phase 1 MAD study for DT-216 in FA, where we assess clinical outcomes such as repeat-dose safety and distribution of DT-216 in muscle, which are important for planning the Phase 2 development. Furthermore, a planned IND for DT-168 for FECD, and progress on promising preclinical programs, stand to confirm the immense potential of our platform.

Bringing forward unprecedented and potentially transformative new therapeutic technology such as GeneTAC™ molecules requires conviction in science, experience, diligence, and perseverance. I am thankful to our entire Design team, our collaborators, investors, and our shareholders for their vision and resolve to deliver on the promise of the potential transformational therapeutics that we are developing. Most importantly, on behalf of our entire team, I'd like to extend our gratitude to the patients, families, and the larger community who remind us daily of the great need for treatments for people living with serious genetic conditions.

We look forward to the year ahead and will keep you apprised of our progress.



João Siffert, M.D.
President and Chief Executive Officer

Forward-looking statements

Statements in this letter that are not purely historical in nature are “forward-looking statements” within the meaning of the Private Securities Litigation Reform Act of 1995. These statements include, but are not limited to, statements related to: projections from early-stage programs, preclinical data and early-stage clinical data; the potential of small molecules to modulate expression of specific genes without irreversible gene therapy or gene editing; the design and potential benefits of our GeneTAC™ small molecules; the timing for reporting initial data from the MAD Phase 1 study in DT-216; our plans to submit an IND for DT-168 and initiate a Phase 1 trial and the timing thereof; the development advantages of small molecules on our programs; our expected completion of IND-enabling studies and the timing thereof; the therapeutic potential of DT-216; the potential benefits of restoring FXN in FA patients; Design’s FECD program and its potential

therapeutic benefits and advantages; and the potential of our GeneTAC™ portfolio to address other serious nucleotide repeat expansion-driven monogenic diseases. Because such statements are subject to risks and uncertainties, actual results may differ materially from those expressed or implied by such forward-looking statements. Words such as "believes," "designed to," "anticipates," "look forward to," "planned," "expects," "estimate," "intends," "will," "goal," "potential," "project" and similar expressions are intended to identify forward-looking statements. These forward-looking statements are based upon Design's current expectations and involve assumptions that may never materialize or may prove to be incorrect. Actual results and the timing of events could differ materially from those anticipated in such forward-looking statements as a result of various risks and uncertainties, which include, without limitation, risks associated with conducting a clinical trial and patient enrollment, which is affected by many factors, and any difficulties or delays encountered with such clinical trial or patient enrollment may delay or otherwise adversely affect Design's MAD Phase 1 clinical study for DT-216; the process of discovering and developing therapies that are safe and effective for use as human therapeutics and operating as a development stage company; Design's ability to develop, initiate or complete preclinical studies and clinical trials for its product candidates; the risk that promising early research or clinical trials do not demonstrate safety and/or efficacy in later preclinical studies or clinical trials; changes in Design's plans to develop its product candidates; uncertainties associated with performing clinical trials, regulatory filings and applications; risks associated with reliance on third parties to successfully conduct clinical trials and preclinical studies; Design's ability to raise any additional funding it will need to continue to pursue its business and product development plans; regulatory developments in the United States and foreign countries; Design's reliance on key third parties, including contract manufacturers and contract research organizations; Design's ability to obtain and maintain intellectual property protection for its product candidates; Design's ability to recruit and retain key scientific or management personnel; and competition in the industry in which Design operates, which may result in others discovering, developing or commercializing competitive products before or more successfully than Design. For a more detailed discussion of these and other factors, please refer to the "Risk Factors" in Design's Annual Report on Form 10-K for the fiscal year ended December 31, 2022. You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof. All forward-looking statements are qualified in their entirety by this cautionary statement and Design undertakes no obligation to revise or update any statements in this letter to reflect events or circumstances after the date hereof, except as required by law.

**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 001-40288

Design Therapeutics, Inc.

(Exact name of Registrant as specified in its Charter)

Delaware

(State or other jurisdiction of
incorporation or organization)

6005 Hidden Valley Road, Suite 110

Carlsbad, California

(Address of principal executive offices)

82-3929248

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

92011

(Zip Code)

Registrant's telephone number, including area code: (858) 293-4900

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, \$0.0001 par value per share	DSGN	The Nasdaq Global Select Market

Securities registered pursuant to Section 12(g) of the Act: **None**

Indicate by check mark if the Registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes No

Indicate by check mark if the Registrant is not required to file reports pursuant to Section 13 or 15(d) of the Act. Yes No

Indicate by check mark whether the Registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the Registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes No

Indicate by check mark whether the Registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the Registrant was required to submit such files). Yes No

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer Accelerated filer

Non-accelerated filer Smaller reporting company

Emerging growth company

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

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

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 Common Stock held by non-affiliates of the Registrant, based on the closing price of the shares of common stock on The Nasdaq Global Select Market on June 30, 2022, the last business day of the Registrant's most recently completed second quarter, was approximately \$372,547,056.

The number of shares of Registrant's Common Stock outstanding as of March 9, 2023 was 55,943,314.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive proxy statement for its 2022 Annual Meeting of Stockholders, which the registrant intends to file pursuant to Regulation 14A with the Securities and Exchange Commission no later than May 1, 2023, are incorporated by reference into Part III of this Annual Report on Form 10-K.

Table of Contents

	<u>Page</u>
PART I	
Item 1. Business	5
Item 1A. Risk Factors	45
Item 1B. Unresolved Staff Comments	105
Item 2. Properties	105
Item 3. Legal Proceedings	105
Item 4. Mine Safety Disclosures	105
PART II	
Item 5. Market for Registrant’s Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities	106
Item 6. [Reserved]	106
Item 7. Management’s Discussion and Analysis of Financial Condition and Results of Operations	107
Item 7A. Quantitative and Qualitative Disclosures About Market Risk	116
Item 8. Financial Statements and Supplementary Data	F-1
Item 9. Changes in and Disagreements With Accountants on Accounting and Financial Disclosure	112
Item 9A. Controls and Procedures	112
Item 9B. Other Information	112
Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections	112
PART III	
Item 10. Directors, Executive Officers and Corporate Governance	113
Item 11. Executive Compensation	113
Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters	113
Item 13. Certain Relationships and Related Transactions, and Director Independence	113
Item 14. Principal Accounting Fees and Services	113
PART IV	
Item 15. Exhibits, Financial Statement Schedules	114
Item 16. Form 10-K Summary	115

PART I

Special Note Regarding Forward-Looking Statements

This Annual Report on Form 10-K and the information incorporated herein by reference contain forward-looking statements that involve risks and uncertainties. We make such forward-looking statements pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995 and other federal securities laws. All statements other than statements of historical facts contained in this Annual Report are forward-looking statements. In some cases, you can identify forward-looking statements by words such as “anticipate,” “believe,” “contemplate,” “continue,” “could,” “estimate,” “expect,” “intend,” “may,” “plan,” “potential,” “predict,” “project,” “seek,” “should,” “target,” “will,” “would,” or the negative of these words or other comparable terminology. These forward-looking statements include, but are not limited to, statements about:

- our plans to research, develop and commercialize our product candidates;
- the initiation, progress, success, cost and timing of our preclinical studies, clinical trials and product development activities;
- the therapeutic potential of our product candidates, and the disease indications for which we intend to develop our product candidates;
- our ability and timing to advance our product candidates into, and to successfully initiate, conduct, enroll and complete, clinical trials;
- our ability to manufacture our product candidates for clinical development and, if approved, for commercialization, and the timing and costs of such manufacture;
- the performance of third parties in connection with the development and manufacture of our product candidates, including third parties conducting our preclinical studies and clinical trials as well as third-party suppliers and manufacturers;
- our ability to obtain funding for our operations, including funding necessary to initiate and complete clinical trials of our product candidates;
- the size and growth of the potential markets for our product candidates and our ability to serve those markets;
- the potential scope, duration and value of our intellectual property rights;
- our ability, and the ability of our licensors, to obtain, maintain, defend and enforce intellectual property rights protecting our platform technologies and product candidates, and our ability to develop and commercialize our product candidates without infringing the proprietary rights of third parties;
- our ability to recruit and retain key personnel; and
- the effects of macroeconomic factors on our operations; and
- other risks and uncertainties, including those described under Part I, Item 1A, "Risk Factors" of this Annual Report.

Any forward-looking statements in this Annual Report reflect our current views with respect to future events or to our future 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. Factors that may cause actual results to differ materially from current expectations include, among other things, those listed under Part I, Item 1A, “Risk Factors” of this Annual Report. 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 Annual Report, 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 and you are cautioned not to unduly rely upon these statements.

Given these uncertainties, you should not place undue reliance on these forward-looking statements. Except as required by law, we assume no obligation to update or revise these forward-looking statements for any reason, even if new information becomes available in the future.

Unless the context otherwise indicates, references in this Annual Report to the terms "Design", "the Company", "we", "our", and "us" refer to Design Therapeutics, Inc., and references to our "common stock" refers to our voting common stock.

Trademarks and Service Marks

“Design Therapeutics,” “Design,” “GeneTAC,” the Design logo and other trademarks, trade names or service marks of Design Therapeutics, Inc. appearing in this Annual Report on Form 10-K are the property of Design Therapeutics, Inc. All other trademarks, trade names and service marks appearing in this Annual Report on Form 10-K are the property of their respective owners.

Summary of Risks Associated With Our Business

An investment in shares of our common stock involves a high degree of risk. Below is a list of the more significant risks associated with our business. This summary does not address all of the risks that we face. Additional discussion of the risks listed in this summary, as well as other risks that we face, are set forth under “Risk Factors” under Part I, Item 1A of this Annual Report. Some of the material risks associated with our business include the following:

- We have a limited operating history, have incurred net losses since our inception, and anticipate that we will continue to incur significant losses for the foreseeable future. We may never generate any revenue or become profitable or, if we achieve profitability, may not be able to sustain it.
- We are early in our development efforts and we have only one product candidate in clinical development, with all other research programs still in the preclinical or discovery stage. We have a limited history of conducting clinical trials to test our product candidates in humans.
- Preclinical and clinical development involves a lengthy and expensive process with uncertain timelines and outcomes, and results of preclinical studies and clinical trials may not be predictive of future trial results. If development of our programs is unsuccessful or delayed, we may be unable to obtain required regulatory approvals and be unable to commercialize our product candidates on a timely basis, if at all.
- Our product candidates are based on novel technologies, which make it difficult to predict the timing, results and cost of product candidate development and likelihood of obtaining regulatory approval.
- Our product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, cause us to suspend or discontinue our ongoing or planned clinical trials, limit the commercial profile of an approved label, or result in significant negative consequences following marketing approval, if any.
- The regulatory approval process is lengthy, expensive and uncertain, and we may be unable to obtain regulatory approval for our product candidates under applicable regulatory requirements. The denial or delay of any such approval would delay commercialization of our product candidates and adversely impact our ability to generate revenue, our business and our results of operations.
- A health epidemic or pandemic could adversely impact our business and affect our operations, as well as the business or operations of our manufacturers or other third parties with whom we conduct business.
- We face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than we do.
- We may rely on third parties to conduct, supervise, and monitor our ongoing and planned clinical trials and perform some of our research and preclinical studies. If these third parties do not satisfactorily carry out their contractual duties or fail to meet expected deadlines, our development programs may be delayed or subject to increased costs, each of which may have an adverse effect on our business and prospects.

- We contract with third parties for the manufacturing and supply of our product candidates for use in preclinical testing and clinical trials, which supply may become limited or interrupted or may not be of satisfactory quality and quantity.
- Any approved products may fail to achieve the degree of market acceptance by physicians, patients, hospitals, healthcare payors and others in the medical community necessary for commercial success.
- If the market opportunities for any of our product candidates are smaller than we believe they are, our revenue may be adversely affected, and our business may suffer.
- If any of our product candidates are approved for marketing and commercialization and we are unable to establish sales and marketing capabilities or enter into agreements with third parties to sell and market our product candidates, we will be unable to successfully commercialize our product candidates if and when they are approved.
- We may not realize the benefits of any acquisitions, in-license or strategic alliances that we enter into.
- We may wish to form collaborations in the future with respect to our product candidates, but may not be able to do so or to realize the potential benefits of such transactions, which may cause us to alter or delay our development and commercialization plans.
- We are highly dependent on our key personnel, and if we are not successful in attracting and retaining highly qualified personnel, we may not be able to successfully implement our business strategy.
- Our business operations and current and future relationships with investigators, health care professionals, consultants, third-party payors and customers are subject, directly or indirectly, to federal and state healthcare fraud and abuse laws, transparency laws and other healthcare laws and regulations. If we are unable to comply, or have not fully complied, with such laws, we could face substantial penalties.
- If we are unable to obtain and maintain sufficient intellectual property protection for our platform technologies and product candidates, or if the scope of the intellectual property protection is not sufficiently broad, our competitors could develop and commercialize products similar or identical to ours, and our ability to successfully commercialize our products may be adversely affected.
- We may not be able to protect our intellectual property rights throughout the world.
- We may rely on trade secrets and proprietary know-how which can be difficult to trace and enforce and, if we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.
- The price of our common stock could be subject to volatility related or unrelated to our operations.

Item 1. Business.

As used in this Annual Report on Form 10-K, unless the context indicates or otherwise requires, "Design," "our company," "we," "us," and "our" refer to Design Therapeutics, Inc., a Delaware corporation.

Overview

We are a clinical-stage biopharmaceutical company pioneering the research and development of GeneTAC™ molecules, which are a novel class of small-molecule gene targeted chimera therapeutic candidates designed to be disease-modifying by addressing the underlying cause of diseases caused by inherited nucleotide repeat expansion mutations. Certain diseases caused by inherited nucleotide repeat expansion, such as Friedreich ataxia (FA) and fragile X syndrome, can result in reduced gene expression and deficiency of vital proteins; in other diseases, such as myotonic dystrophy type-1 (DM1), Fuchs endothelial corneal dystrophy (FECD), and Huntington disease, the nucleotide repeat expansions result in the generation of toxic gene products, often associated with pathological nuclear foci and broad splicing disruptions. Our GeneTAC™ small molecules are designed to selectively target expanded genetic repeat sequences, modulate gene expression either by dialing up or down mRNA transcription, depending on the cause of the disease, and restore cellular health. As a platform, we believe that GeneTAC™ molecules have broad potential applicability across currently unaddressed degenerative, monogenic nucleotide repeat expansion diseases affecting millions of individuals worldwide.

In preclinical studies for our lead program in FA, we have observed restoration of frataxin (FXN) levels in multiple cell types from FA patients and an *in vivo* murine model of FA using our FA GeneTAC™ molecules. At doses that were observed to be well tolerated in rodents and non-human primates, FA GeneTAC™ molecules achieved biodistribution to brain and heart, key organs affected by FA, at concentrations that exceeded those observed to restore FXN levels in FA patient cells. Further, and consistent with this favorable target-organ biodistribution, we observed increased endogenous FXN expression in the brain and heart in an animal model of FA after treatment with our FA GeneTAC™ molecules. In February 2022, the Investigational New Drug Application (IND) for our lead FA GeneTAC™ development candidate (DT-216) was cleared by the U.S. Food and Drug Administration (FDA). Additionally, the FDA has granted Fast Track designation to DT-216 for the treatment of patients with FA. In March 2022, we completed dosing in the first cohort for the single-ascending dose (SAD) Phase 1 clinical trial of DT-216. In December 2022, we reported positive initial data from the SAD clinical trial showing that DT-216 was generally well-tolerated and able to overcome the FXN transcription impairment that causes FA, with a greater than two-fold increase in FXN mRNA in the cohort with the highest response. These data support the continued advancement of DT-216 in the ongoing multiple-ascending dose (MAD) Phase 1 clinical trial of DT-216 and the anticipated Phase 2 clinical trial in FA patients, which is expected to begin in the second half of 2023.

In December 2022, we nominated our second GeneTAC™ development candidate (DT-168), an eye drop for the treatment of FECD. When tested *in vitro* in FECD patient-derived corneal endothelial cells, our FECD GeneTAC™ molecules led to robust reductions in the pathogenic nuclear RNA foci and corrected key mis-spliced transcripts to levels observed in control corneal endothelial cells from unaffected donors. DT-168 was well tolerated and distribution of DT-168 was observed in and through the cornea in animal models after administration via eye drop. We believe these preclinical data support the potential of our novel GeneTAC™ small molecules to correct the most common underlying genetic cause of FECD, and we plan to advance this research program through additional preclinical studies and submit an IND for DT-168 in the second half of 2023.

Our third program based on the GeneTAC™ platform is DM1. Multiple DM1 GeneTAC™ molecules elicited robust reduction of nuclear foci and correction of splicing defects in DM1 patient muscle cells. Preclinical *in vivo* studies demonstrated distribution of DM1 GeneTAC™ molecules to key target tissues including skeletal muscle and heart, achieving tissue concentrations of intact DM1 GeneTAC™ molecule that reduced pathogenic nuclear foci to normal levels in our *in vitro* experiments. We expect to complete IND-enabling studies and submit an IND in 2024.

We have continued to make significant progress in advancing our GeneTAC™ portfolio in preclinical studies to address other serious nucleotide repeat expansion-driven monogenic diseases, and intend to declare additional product candidates as they progress towards the clinic.

We believe the structure and mechanism of action of our GeneTAC™ molecules may offer the disease-modifying potential of genomic therapeutics, while also offering broad tissue biodistribution, resolution of aberrant gene expression preserving endogenous regulatory control elements, and leveraging established manufacturing, regulatory, and distribution frameworks for small molecules.

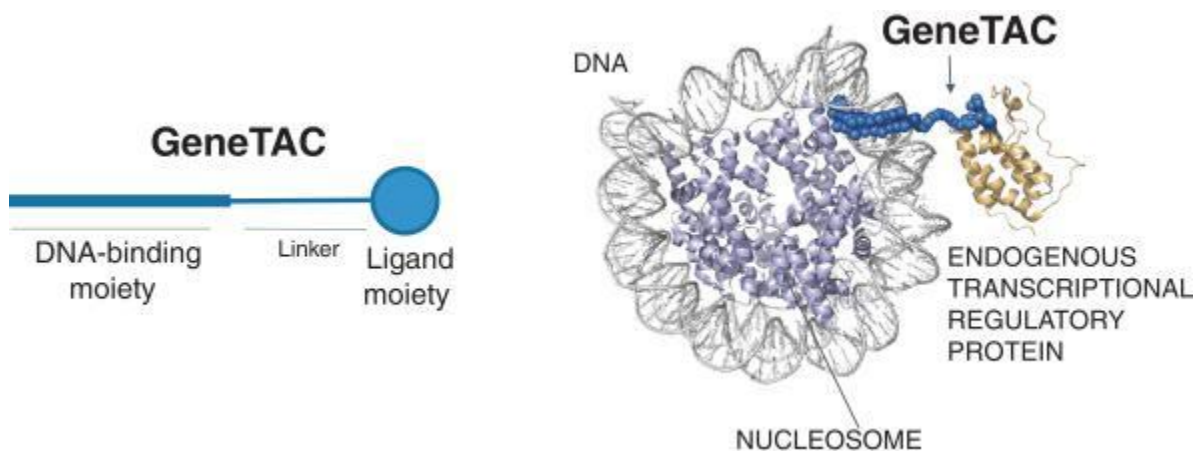
Our GeneTAC™ Platform

We utilize our proprietary GeneTAC™ platform to design and develop therapeutic candidates for inherited diseases driven by nucleotide repeat expansion. Individuals with nucleotide repeat expansion diseases are born with abnormally expanded stretches of specific nucleotide sequences, often with hundreds to thousands of excess repeats present in the mutant gene. Higher number of excess repeats can lead to more severe, and sometimes a more rapidly progressive form of disease. Nucleotide repeat expansion has been identified as the underlying cause of more than 40 debilitating degenerative diseases impacting millions of people. Currently, there are no approved therapeutic options that address the cause of any nucleotide repeat expansion diseases.

Specific DNA sequences of a gene can generate RNA through a process called transcription. The RNA is, in turn, used as a template to make the proteins that control cellular functions in a process called translation. Combined, transcription and translation are responsible for gene expression. Individuals who have a nucleotide repeat expansion in the DNA can experience different alterations of transcription. In some diseases such as FA, the transcription machinery stalls at the abnormally expanded repeat sequence leading to insufficient production of a critical protein called FXN. In other cases, such as in DM1, the abnormal RNA transcript arising from the nucleotide repeat expansion mutation is misprocessed, leading to a cascade of downstream toxicity and cellular dysfunction.

GeneTAC™ molecules represent a novel class of small molecules designed to act on a diverse array of diseases and selectively target genetic repeat sequences, modulate gene expression either by dialing up or down mRNA transcription, and restore cellular health. We have developed a proprietary framework that combines our understanding of medicinal chemistry and structure-activity relationships that allow us to design DNA-targeting moieties that are connected via a linker to ligand moieties that engage and modulate the transcriptional machinery. GeneTAC™ molecules are heterobifunctional, meaning that they are comprised of two principal moieties that are each designed to have a unique function:

- **DNA-Targeting Moiety:** one end of the GeneTAC™ molecule is a DNA targeting molecule that has been designed to recognize and target the molecule to the specific nucleotide repeat sequence of interest (e.g. the repeated GAA sequence seen in the first intron of the FXN gene seen in FA or the CTG repeat in the 3' non-coding region of the dystrophy myotonic protein kinase (DMPK) gene seen in DM1).
- **Ligand Moiety:** the other end of the molecule is designed to interact with the endogenous proteins that can regulate transcription to either dial up or dial down the expression of an individual gene.



The structures of the GeneTAC™ molecules are designed to enable them to act specifically at the site of the disease-causing nucleotide repeat expansion by targeting the mutant allele and modulating the transcriptional machinery in a cell. Consequently, the cell can resume gene expression and production of normal protein isoforms that remain under normal physiological control. The versatility of the GeneTAC™ platform allows us to design GeneTAC™ molecules toward a specific nucleotide repeat expansion target, regardless of repeat number, and tailor it to address the underlying disease-specific dysfunction in gene regulation in one of the following ways:

- **Restoration of Transcription:** In diseases where the expanded nucleotide repeat structure can cause endogenous transcription machinery to stall, which leads to an insufficient amount of protein production, GeneTAC™ molecules can be designed to target the desired loci in the genome and engage the endogenous transcriptional machinery with the goal of restoring normal levels of full-length pre-mRNAs. In FA, for example, where the expanded triplet repeat occurs in an intron, a non-coding region of the gene, the abnormally long nucleotide sequence is spliced out of the pre-mRNA thus enabling normal production of natural protein isoforms according to existing physiologic regulatory control.
- **Reduction of Toxic Gene Product Levels:** Another type of nucleotide repeat expansion disease occurs when the transcription process results in the accumulation of toxic gene products (e.g. DM1, Huntington disease, FECD), and in some cases the formation of nuclear foci, leading to multiple downstream cellular dysfunctions. In these cases, a single copy of expanded repeat containing allele is sufficient to cause the disease. Our GeneTAC™ molecules are designed to selectively target the abnormally expanded nucleotide repeat to block the formation of the downstream toxic gene product and restore cellular function without interfering with the gene expression of the normal allele.

Our understanding of the properties of the GeneTAC™ molecules is based on data-driven assessments of compounds we have designed and synthesized, as well as experience with our most advanced compounds for FA, FECD and DM1 tested *in vitro* and *in vivo*. We continue to develop know-how of diverse configurations of DNA targeting, linker, and ligand moieties that drive the drug properties of molecules which are best suited to be developed for treating the underlying cause of each specific disease. This understanding of GeneTAC™ chemistry has enabled us to generate multiple candidates designed to have optimal potential therapeutic and drug characteristics.

Our Programs

We are developing a portfolio of GeneTAC™ product candidates designed to address genetic diseases driven by inherited nucleotide repeat expansions that have urgent medical need and where no approved disease-modifying treatments are currently available. Because GeneTAC™ molecules are designed to be a novel class of disease-modifying small molecule therapeutic candidates, we have selected disease programs where we believe the underlying cause is amenable to intervention using our technology and prioritized our development efforts where we believe there is a clear and efficient path to advance these candidates through clinical development, with the goal of providing a disease-modifying therapy for patients.

Our lead candidates and early development programs are summarized in the table below:

Figure 1: GeneTAC™ Pipeline

DEVELOPMENT PROGRAMS	NEXT ANTICIPATED MILESTONE	EXPECTED TIMING
Friedreich ataxia (GAA) – DT-216	Data from MAD trial	Mid-2023
	Initiate phase 2	2H 2023
Fuchs endothelial corneal dystrophy (FECD; CTG) – DT-168	IND	2H 2023
Myotonic dystrophy type 1 (CTG)	IND	2024

FA Program Overview (DT-216)

Our FA program is focused on the development of a potentially disease-modifying treatment. FA is a devastating monogenic, autosomal recessive progressive disease where over 95% of cases are caused by homozygous guanine-adenine-adenine (GAA) triplet repeat expansions in the first intron of the FXN gene, which encodes the mitochondrial protein FXN. The disease is characterized by spinocerebellar ataxia, dysarthria, pyramidal weakness, deep sensory loss, hypertrophic cardiomyopathy, skeletal abnormalities, and diabetes mellitus. Clinical onset occurs most often around puberty, leads to severe disability by early adulthood, with substantial functional loss, wheelchair dependence, and loss of quality of life. Affected individuals have reduced life expectancy, with many premature deaths caused by complications of the cardiomyopathy at about the end of the fourth decade of life.

The estimated prevalence of FA is 1 in 40,000-50,000, affecting more than 5,000 individuals living in the United States and more than 20,000 in Europe. Our FA GeneTAC™ candidate is designed to address the genetic basis of the disease by restoring functional FXN protein levels. In December 2022, we reported positive initial data from the SAD clinical trial showing that DT-216 was generally well-tolerated and able to overcome the FXN transcription impairment that causes FA. We anticipate the continued advancement of our first product candidate in the ongoing MAD Phase 1 clinical trial and the Phase 2 clinical trial, which is expected to begin in the second half of 2023.

FECD Program Overview (DT-168)

Our FECD program is focused on the development of a potentially disease-modifying medical treatment for FECD. FECD is characterized by progressive degeneration of the corneal endothelium and subsequent loss of vision. This genetic eye disease affects millions of people in the U.S., with approximately 75% of cases caused by a CTG trinucleotide repeat expansion within the transcription factor 4 (TCF4) gene, leading to the formation of pathogenic RNA foci, global splicing dysregulation, cellular dysfunction, and eventual loss of corneal endothelial cells. Due to the lack of disease-modifying therapies approved for FECD, corneal surgery is currently the only approved procedure used to restore vision. Our approach utilizes our FECD GeneTAC™ molecules to selectively target the expanded CTG repeats in the TCF4 gene to reduce RNA foci formation and mis-splicing. We believe our preclinical data to date supports the potential of our FECD GeneTAC™ small molecules to correct the most common underlying genetic cause of FECD, and we plan to submit an IND for DT-168 in the second half of 2023.

DM1 Program Overview

Our DM1 program is focused on the development of a potentially disease-modifying treatment for DM1. DM1 is a monogenic, autosomal dominant, progressive neuromuscular disease that affects skeletal muscle, heart, brain, and other organs. The cardinal features include muscle weakness, myotonia (slow muscle relaxation), and early cataracts. In addition, affected individuals often experience cardiac arrhythmias, changes in neuropsychological function, and gastrointestinal symptoms. DM1 is caused by a mutation in the DMPK gene and is estimated to have a genetic prevalence of 1 in 2,300-8,000 people, affecting more than 70,000 people in the United States and more than 90,000 people in Europe. Our DM1 GeneTAC™ molecules are designed to address the genetic cause of the disease by preventing the expression of mutant gene product and consequently of pathogenic nuclear foci. We expect to complete IND-enabling studies and submit an IND in 2024.

Research Program Overview

We are also advancing our GeneTAC™ product candidate portfolio into development in other serious nucleotide repeat expansion-driven monogenic diseases, such as fragile X syndrome, spinocerebellar ataxias, Huntington disease, spinobulbar muscular atrophy and C9orf72-amyotrophic lateral sclerosis/frontotemporal dementia. Many of these monogenic diseases have overlapping triplet repeat expansions, including CTG repeats that cause DM1, allowing for the accumulating knowledge on how to design novel molecules to be applied across multiple diseases also caused by CTG and CAG repeat expansions. Additionally, our medicinal chemistry experiences with GeneTAC™ molecules allow us to more rapidly design GeneTAC™ molecules for additional proposed indications.

Our Strategy

We aim to leverage our GeneTAC™ platform to design, develop and commercialize a pipeline of disease-modifying therapeutic candidates designed to treat a wide range of inherited nucleotide repeat expansion diseases for which there is urgent unmet medical need. In order to achieve our goal, we intend to:

- ***Advance our Lead Program in FA Through Clinical Development to Offer Meaningful Patient Benefit.*** FA is a serious monogenic degenerative disease for which there are currently no available disease-modifying treatments. Our FA GeneTAC™ molecules are specifically designed to restore levels of FXN, the underlying cause of FA. Restoration of FXN has been shown to improve FA-like symptoms in animal models. We believe that demonstrating clinical proof of concept by restoring FXN expression in FA patients may confirm the therapeutic potential of our FA GeneTAC™ molecules and underscore the broader potential of our GeneTAC™ platform. We have completed IND-enabling safety studies in both rats and non-human primates and received FDA clearance of our IND in late February 2022. In March 2022, we initiated the SAD Phase 1 clinical trial in patients with FA. In December 2022, we reported positive initial data from the SAD clinical trial showing that DT-216 was generally well-tolerated and able to overcome the FXN transcription impairment that causes FA, with a greater than two-fold increase in FXN mRNA in the cohort with the highest response. These data support the continued advancement of DT-216 in the ongoing MAD Phase 1 clinical trial of DT-216 and the anticipated Phase 2 clinical trial in FA patients, which is expected to begin in the second half of 2023.
- ***Advance our FECD Program Through Clinical Development to Offer Meaningful Patient Benefit.*** FECD is a genetic eye disease characterized by bilateral degeneration of corneal endothelial cells and progressive loss of vision, for which the only approved option for treatment is corneal surgery. DT-168 is our FECD GeneTAC™ small molecule designed to target the CTG repeats in the TCF4 gene and selectively block transcription of the expansion-containing allele. IND-enabling studies are ongoing and we expect to submit an IND for DT-168 in the second half of 2023.

- **Advance our DM1 Program Through Clinical Development to Offer Meaningful Patient Benefit.** DM1 is a serious monogenic degenerative disease for which there are currently no available treatments. Our DM1 GeneTAC™ molecules are specifically designed to reduce the formation of CUG repeat hairpin structures that trap splicing factors and form pathogenic nuclear foci that cause DM1. Blocking the formation of CUG foci has demonstrated phenotypic benefit. We believe that demonstrating clinical proof of concept by reducing the repeat hairpin structures in DM1 patients may confirm the therapeutic potential of this candidate. We expect to complete IND-enabling studies and submit an IND in 2024.
- **Leverage our GeneTAC™ Platform to Expand our Pipeline and Address Additional Nucleotide Repeat Expansion Diseases with Significant Unmet Medical Need.** There remains a significant unmet medical need for all nucleotide repeat expansion diseases. We plan to advance our GeneTAC™ portfolio to address the underlying cause of other serious nucleotide repeat expansion-driven monogenic diseases, which may include fragile X syndrome, spinocerebellar ataxias, Huntington disease, spinobulbar muscular atrophy and C9orf72-amyotrophic lateral sclerosis/frontotemporal dementia, the majority of which have no approved disease-modifying treatments.
- **Selectively Enter Into Strategic Collaborations.** Given the broad potential of our GeneTAC™ platform, we may explore collaborations in select disease areas or geographic regions that are better served by the resources or specific expertise of a strategic partner to accelerate the development and commercialization of our GeneTAC™ product candidates.
- **Independently Commercialize any Approved Products in Indications and Geographies Where we Believe we can Maximize Value.** We intend to commercialize our product candidates that receive regulatory approval in indications and geographies where we believe we can maximize value by commercializing on our own.
- **Establish a Leadership Position in Genetic Diseases by Continuing to Build and Leverage our Relationships with the Key Opinion Leaders, Physicians, and Patients.** We have an established advisory network of pharmaceutical research and development experts, scientists, clinicians and patient organizations in areas relevant to our programs. We have continued to grow our network as needed to inform our programs with the most up to date data and practices that might enhance our ability to effectively bring potentially life saving treatments to patients in need.

Our History and Team

Our company was created to design, develop and commercialize a novel class of small molecule therapeutic candidates (GeneTAC™ molecules) designed to directly address the underlying basis of genetic disease. To achieve this goal, we have assembled a management team with extensive experience in the design, development and commercialization of drugs for serious diseases.

Our company was started by Pratik Shah, Ph.D. and Aseem Z. Ansari, Ph.D. Dr. Shah, our Co-Founder and Executive Chairperson, has more than 30 years of experience founding and leading biopharmaceutical companies and healthcare investment decisions. Dr. Ansari, our Co-Founder, is an internationally recognized pioneer in transcriptional regulation and DNA targeting molecules and the chair of the Department of Chemical Biology and Therapeutics at St. Jude Children’s Research Hospital. João Siffert, M.D., our President and Chief Executive Officer, has more than 20 years of leadership experience in biopharmaceutical companies and clinical medicine. Prior to Design, Dr. Siffert led a publicly traded biotech company developing gene and cell therapies for devastating degenerative diseases, and previously led research and development organizations in the United States and Europe, including programs that received regulatory approvals followed by commercial launches. Sean Jeffries, Ph.D., our Chief Operating Officer, brings over 20 years of experience in business development, portfolio management, and research and development strategy for both emerging and large biopharmaceuticals companies.

Background on Genomic Medicines

What is Genetic Disease?

Genetic diseases arise when a change to the DNA, called a mutation, disrupts normal cellular functioning. These mutations can range from alteration of a single nucleotide in an individual's DNA to major abnormalities affecting many genes or even entire chromosomes. When a mutation occurs in a single gene, the disease is referred to as a monogenic disease. More than 10,000 monogenic diseases have been identified and many are serious conditions that collectively affect millions of people globally, most of which have no effective therapeutic options.

What is Genomic Medicine?

Genomic medicines are created based on understanding of genetic causes of disease, targeting specific defects at the genetic level with the potential to address the underlying cause of disease and restore cellular function.

Technical and scientific advances in genomics have identified possible genetic targets for therapeutic interventions. Several approaches have been developed to address diseases caused by genetic mutations, including oligonucleotides, mRNA, gene therapy and gene editing. While these technologies have led to numerous product candidates over the last decade, significant challenges have limited their utility in the clinic as a result of:

- immunogenicity that creates safety concerns and limits activity and re-dosing;
- unregulated gene expression;
- off-target effects;
- limitations of dose adjustments/silencing;
- limitations and heterogeneity of biodistribution; and
- challenges with consistency, quality and scalability of manufacturing.

Advantages of Our Platform

We are using our GeneTAC™ platform to develop small molecule genomic medicine candidates that are designed to offer precise modulation of gene transcription. We believe that the GeneTAC™ platform may offer several potential mechanistic and development advantages over other genomic medicine modalities, including:

- GeneTAC™ small molecules may be more tolerable over complex biologics because GeneTAC™ molecules are less likely to cause adverse immune reactions;
- GeneTAC™ molecules may be less likely to be immunogenic and therefore have no limitations with re-dosing;
- GeneTAC™ treatment is designed to be reversible;
- GeneTAC™ molecules are designed to act on the transcription machinery of the cell and do not alter the genome;
- GeneTAC™ molecules' modulation of transcription is designed to preserve normal physiological post-transcriptional regulation and protein translation controls;
- GeneTAC™ structure is designed to enable therapeutically active molecules to be deployed directly at the site of disease-causing mutations, which could enhance specificity and potency, and minimize off-target effects;
- GeneTAC™ molecules are designed to enable ongoing dose optimization;
- GeneTAC™ molecules can achieve biodistribution across target organs and into the cell without specialized engineering or delivery technologies;

- GeneTAC™ molecules are synthetically tractable, offering a potentially readily scalable, cost-effective development path that does not require complex customized manufacturing equipment and processes; and
- GeneTAC™ molecules have a modular heterobifunctional structure that is intended to allow us to rationally design novel targeting components for specific DNA sequences, creating a potentially highly efficient discovery engine that could enable us to rapidly expand our portfolio into new disease areas.

By combining the disease-modifying potential of genomic medicines with the drug-like properties, manufacturing and logistics advantages of small molecules, we believe GeneTAC™ molecules could be developed as novel therapeutic options in genetic diseases where disease-modifying treatments have previously been elusive.

Our Portfolio

Friedreich Ataxia

Disease Overview, Prevalence and Current Treatment Landscape

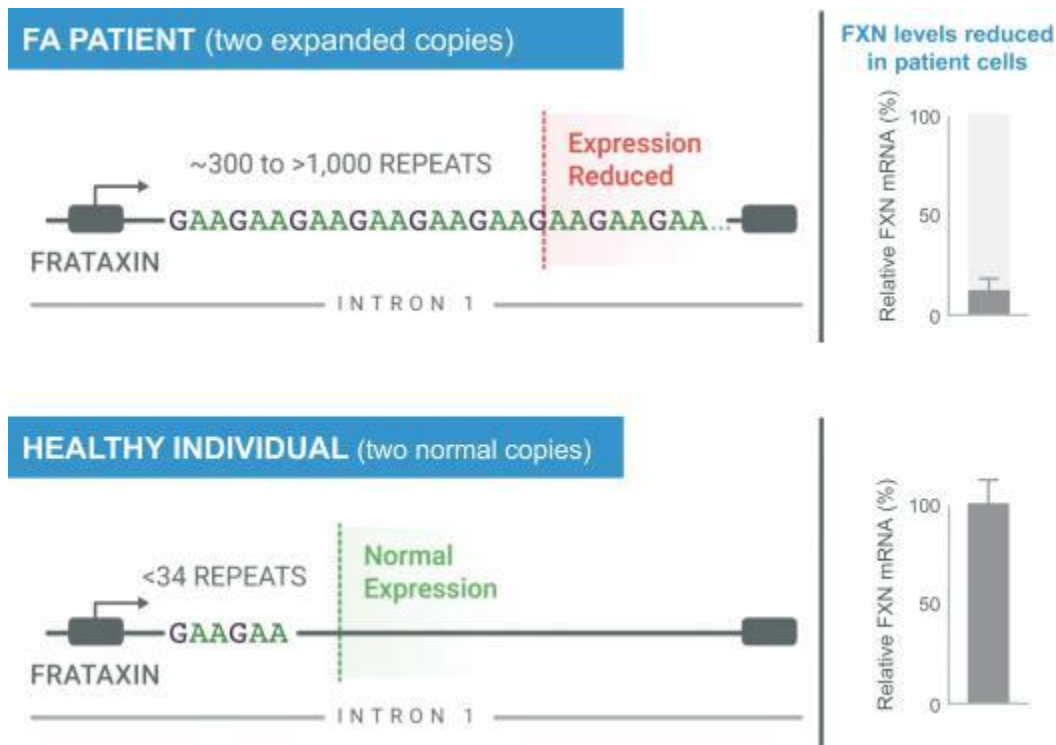
FA is a monogenic, autosomal recessive, progressive multi-system disease that affects organ systems highly dependent on mitochondrial function, eventually leading to neurological, cardiac, and metabolic dysfunction. Clinical manifestations include poor coordination of legs and arms, progressive loss of balance and ability to walk, generalized weakness, loss of sensation, scoliosis, hypertrophic cardiomyopathy and cardiac arrhythmia, and glucose intolerance, including diabetes. FA patients also report impaired vision, hearing and speech. FA significantly impairs quality of life with loss of independence, physical limitations and reduced participation in social activities and work.

The primary cause of mortality (approximately 60% of FA patients) is cardiac arrhythmias or heart failure with the mean life expectancy reduced to approximately 35-40 years.

In over 95% of patients, FA is caused by an inherited homozygous increase in the number of GAA triplet repeats found in the first intron of the FXN gene. The number of repeats ranges from up to approximately 30 GAA repeats in healthy individuals to over several hundred to over 1,000 in FA patients. The expanded triplet repeat results in gene silencing and reduction in capacity to produce the FXN protein, which is required for proper functioning of the mitochondria and ultimately the entire cell. Levels of FXN correlate inversely with disease severity, and when levels are reduced to levels of approximately 25% of normal healthy individuals, iron homeostasis and iron-sulfur cluster synthesis are impaired, leading to general impairment of normal mitochondrial function. Heterozygote carriers typically have approximately half of the FXN levels of normal individuals, but are asymptomatic and hence on average, the doubling of FXN protein levels in FA patients to achieve carrier levels or higher is expected to restore mitochondrial function and provide therapeutic benefit.

The genetic basis for FA is illustrated in Figure 2 below.

Figure 2: Genetic basis for FA



The clinical course of FA is progressive, with most patients presenting in their adolescent years with gait ataxia and scoliosis. About 10 years after disease onset, most patients lose their ability to walk and require a wheelchair because of progressive loss of balance and muscle weakness in the torso and legs. Eventually, muscle weakness in the tongue and throat makes it difficult to swallow and eat, and almost all patients experience some degree of dysarthria (slowing/slurring of speech), which limits communication. Approximately 50% of FA patients develop glucose intolerance and approximately 30% develop diabetes. More than two thirds of FA patients have cardiac abnormalities at baseline including arrhythmia, conduction abnormalities, or hypertrophic cardiomyopathy. Cardiac abnormalities are responsible for approximately 60% of mortality in FA patients. FA significantly reduces life expectancy and impairs quality of life for patients and their families with loss of independence, physical limitations and reduced participation in social activities and work.

The estimated prevalence of FA is 1 in 40,000-50,000, affecting more than 5,000 individuals living in the United States and more than 20,000 in Europe.

On February 28, 2023, Reata Pharmaceuticals announced that the FDA approved omaveloxolone for the treatment of FA in adults and adolescents aged 16 years and older. In addition, there are several product candidates in clinical development but neither omaveloxolone nor any of these product candidates have shown the ability to restore the deficiency in FXN protein, which is the underlying cause of the disease. There remains a high unmet medical need for disease-modifying therapies.

Our Approach

Our FA program is based on GeneTAC™ small molecules consisting of a DNA-targeting moiety designed to target the expanded GAA repeat sequence in the first intron of the FXN gene in FA patients, linked to a ligand moiety designed to recruit an endogenous transcriptional elongation complex to unblock the transcriptional machinery, and restore the production of functional natural FXN proteins to therapeutic levels.

The key advantages of our FA program include the following:

- **Designed to Address the Underlying Cause of the Disease.** FA is caused by reduced FXN protein levels. All disease manifestations are downstream effects of FXN deficiency. Our FA GeneTAC™ molecules are designed to restore FXN levels, thereby restoring normal physiological activity.
- **High Potency Compounds.** Our FA GeneTAC™ molecules have shown high potency and prolonged restoration of FXN levels in preclinical assays in FA patient cells and *in vivo* model of FA.
- **Designed for Efficient Delivery of Drug to the Target Organs.** We have observed good biodistribution and bioavailability for FA GeneTAC™ molecules in multiple animal species, where they reached therapeutically relevant concentrations in the most affected organs such as heart, brain, muscle and spinal cord.

Preclinical Data

We believe that the results of our preclinical studies to date support the hypotheses that FA GeneTAC™ molecules may confer a clinical benefit to FA patients. In *in vitro* experiments in primary cells from FA patients and in neurons and cardiomyocytes derived from FA patient stem cells, robust and durable increases in FXN mRNA and protein restoration was observed following exposure to FA GeneTAC™ molecules, even at low nanomolar (nM) concentrations. In preclinical studies, FA GeneTAC™ molecules achieved therapeutically relevant concentrations in key organs of disease, including the heart, brain, muscle and spinal cord, at doses that were well tolerated in multiple species.

We assessed the FA GeneTAC™ activity in *in vitro* and *in vivo* models of disease, including multiple types of FA patient cells such as primary white blood cells, lymphoblastoid cells, and cardiomyocytes and neurons derived from stem cells. *In vivo* studies were conducted in the Pook800J mouse model, which contains a hemizygous insertion of the human disease allele with approximately 800 GAA repeats onto a genetic background lacking endogenous mouse FXN.

Increase in FXN mRNA and Protein in FA Patient Neurons

Continuous exposure to low doses of an FA GeneTAC™ molecule (10 or 100nM) increased FXN expression in neurons derived from an FA patient stem cell line (Figure 3). Increases in FXN mRNA levels preceded increases in FXN protein, consistent with the typical pattern of gene expression. Of note, the increase in FXN protein levels after continuous treatment with 10 or 100 nM of the FA GeneTAC™ molecule resulted in similar FXN protein levels which were also similar to - and did not exceed - those in a non-FA patient-derived neurons in culture (grey horizontal bar in Figure 3 right panel).

Figure 3: FXN mRNA and protein levels in FA patient neurons

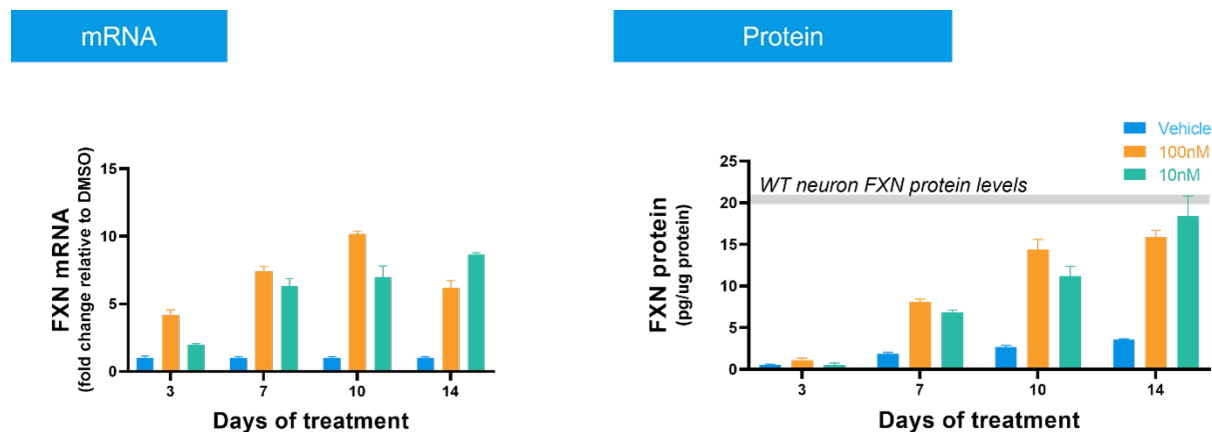


Figure 3. Neurons from an FA patient were incubated with 10 or 100 nM of an FA GeneTAC molecule continuously, and cells were harvested for determination of FXN mRNA (left) or protein (right) levels on Days 3, 7, 10, and 14. Data are depicted as Mean \pm SD (n=3/group). Grey horizontal bar (right panel) indicates range of FXN protein levels in non-FA patient derived neurons on Day 14

In preclinical studies in Pook800J mice, we observed an increase in FXN protein levels in both heart and brain tissue after treatment with FA GeneTACTM molecules.

Distribution and Tolerability of FA GeneTACTM molecules

In preclinical studies in cynomolgus monkeys, repeat intravenous (IV) administration of our FA GeneTACTM molecules at weekly intervals led to exposure in the plasma at concentrations above 10nM for up to 48 hours after the last dose, while exposure in key target organs in the context of functional deficits encountered in FA (Figure 4), including the heart, brain and skeletal muscle, sustained well above concentrations shown to increase FXN mRNA and protein in FA patient cells for at least 7 days after the last dose. FA GeneTACTM molecule was also shown to be well tolerated and resulted in no clinically meaningful changes in hematology, serum biochemistry or histology.

Figure 4: FA GeneTACTM concentration in target tissues of NHPs

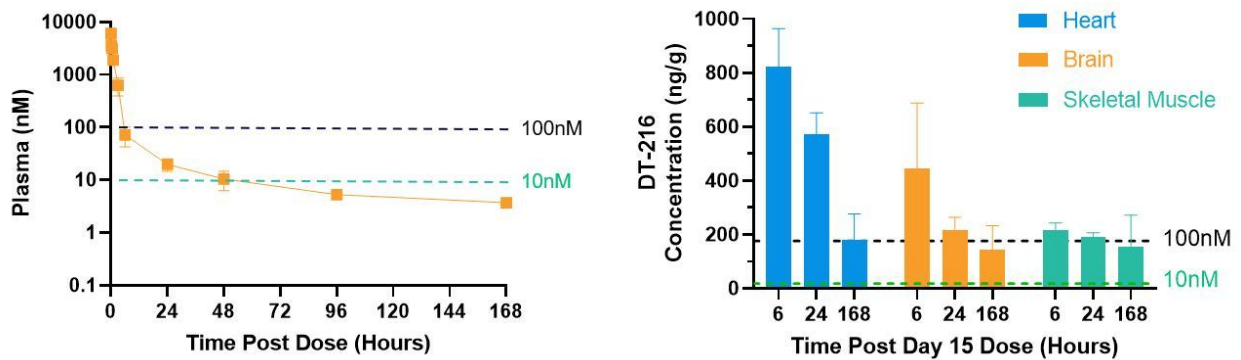


Figure 4. FA GeneTACTM molecule was administered once weekly to male cynomolgus monkeys by IV injection on Days 1, 8, and 15. Plasma and tissues were collected from 2 monkeys at 6, 24, and 168 hours after the Day 15 dose for determination of FA GeneTACTM molecule levels by LC-MS/MS. Data are depicted as the Mean + SE.

Clinical Data

DT-216 Phase 1 SAD Trial Design

The Phase 1 SAD clinical trial was a randomized, double-blind, placebo-controlled study designed to evaluate single doses of DT-216 administered intravenously in adult patients with FA. The primary and secondary study objectives were to evaluate safety and tolerability, and pharmacokinetics (PK) of DT-216 in FA patients. Change in FXN mRNA and protein expression relative to baseline, measured in a circulating subset of white blood cells, known as peripheral blood mononuclear cells (PBMCs), were included as exploratory pharmacodynamic (PD) assessments.

Thirty-nine FA patients (mean age 32 years, 49% female) were dosed across six dose cohorts (5-10 patients per cohort) ranging from 25 mg to 600 mg and were randomized to receive either DT-216 (N=26) or placebo (N=13). All patients were homozygous for a GAA repeat expansion (mean=580, SD=203).

The study protocol was prospectively designed for DT-216 to be administered either as a single dose bolus or as a single dose split-administration on the same day. Patients in Cohorts 1-4 were dosed with a single bolus dose of DT-216 at increasing levels from 25 mg to 200 mg. Patients in Cohort 5 (400 mg) received either a single dose bolus or single dose split administration of DT-216, and all patients in Cohort 6 (600 mg) received a single dose split administration of DT-216. Safety assessments were conducted for at least 30 days post dosing.

Initial data from Phase 1 SAD trial

DT-216 was generally well-tolerated throughout the Phase 1 SAD trial. Findings from Cohorts 1-5 were:

- No treatment-related serious adverse events (SAEs) reported
- 16 (73%) patients on DT-216 and eight (73%) patients on placebo reported at least one treatment-emergent adverse event
- Most adverse events (AEs) were mild and transient; there were no severe AEs
- No clinically significant changes in vital signs, physical exams, electrocardiogram, and clinical safety laboratories (including liver function tests and serum creatinine)
- Three patients on DT-216 had a localized superficial vein thrombosis at the injection site; of which two were mild and one was moderate; and all three were self-limited

Data from Cohort 4 (200 mg) were excluded from the analysis of PK and PD data due to third-party issues with sample handling. PK data were analyzed for patients that were treated with DT-216 in Cohorts 1-3, 5 and 6. Plasma levels of DT-216 increased in an approximately dose-proportional manner, with peak concentrations within minutes, followed by a decrease in plasma levels within several hours.

PD data were available for 33 patients (Cohorts 1-3, 5 and 6, Figure 5). Treatment with a single dose of DT-216 resulted in a 2.24-fold increase in FXN mRNA, at 24 hours post-dose compared with pre-treatment baseline, in the cohort with the highest response ($p < 0.01$ DT-216 [N=3] vs. pooled placebo [N=11]). Treatment with a single dose of DT-216 in all cohorts 100 mg and above resulted in a statistically significant increase in FXN mRNA at 24 hours post dose. Individual patient responses to single doses of DT-216 ranging from 100-600 mg resulted in an increase in FXN mRNA at 24 hours ranging from 1.24 to 2.62-fold. A relationship between plasma exposure and treatment effect was observed in PBMCs (Figure 6).

Figure 5: Greater than two-fold increase in FXN mRNA in PBMCs in cohort with highest response

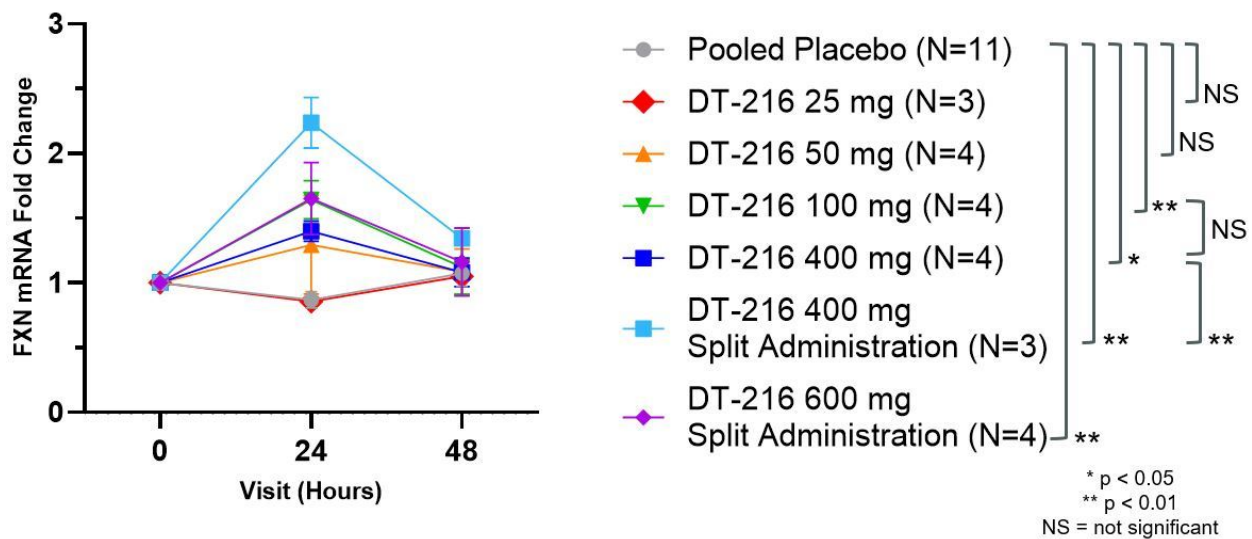
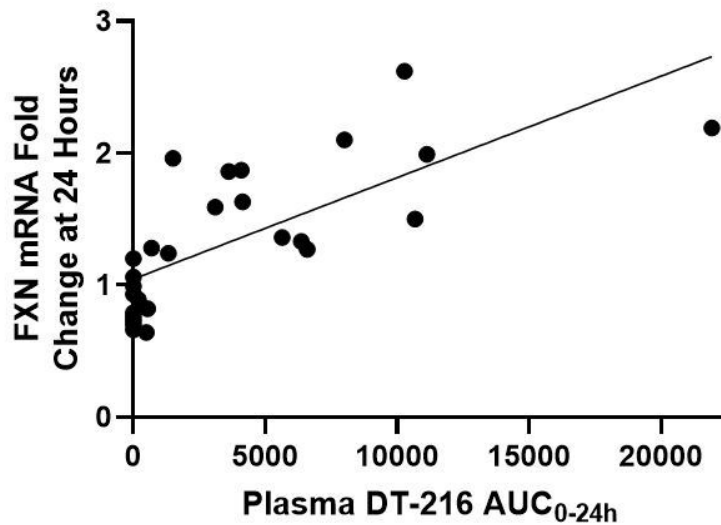


Figure 5. Post-splice FXN mRNA was measured using intron spanning RT-qPCR to detect post-spliced mature mRNA in FA patients at baseline, 24 hours and 48 hours after dosing with DT-216. Pharmacodynamic data from Cohort 4 (200 mg) excluded from analysis due to third-party issues with sample handling. Exploratory statistical analyses were conducted using an ANCOVA model which includes a main effect for the treatment group and the baseline delta Ct as a covariate and compares each active treatment group against the pooled placebo group. The reported p values are based on parametric statistical analysis methods. Non-parametric analyses gave similar results. Bars represent standard error of the mean.

Figure 6: Positive correlation between DT-216 exposure and FXN mRNA response in PBMCs

FXN mRNA fold change at 24 hours vs DT-216 plasma PK (AUC_{0-24h})



FXN mRNA fold change at 24hr vs DT-216 plasma PK slope is significantly positive, nominal p <0.0001; Linear regression with best-fit line

Figure 6: Post-splice FXN mRNA measured using intron spanning RT-qPCR to detect post-spliced mRNA in FA patients at baseline and after DT-216 dosing. Pharmacodynamic data from Cohort 4 (200 mg) excluded from analysis due to third-party issues with sample handling.

As expected with short-term plasma exposure, there was no observed increase in FXN protein from baseline in PBMCs from patients treated with a single dose of DT-216 or placebo. Ex vivo DT-216 treatment for 60 hours of PBMCs isolated pre-treatment from patients enrolled in this trial elicited a doubling of FXN protein levels, showing that, with sufficient duration of exposure to DT-216, an increase in FXN mRNA naturally translated to an increase in FXN protein.

Design is evaluating DT-216 in an ongoing MAD Phase 1 clinical trial designed to evaluate the safety, tolerability, PK, biodistribution and PD effects of three weekly doses of DT-216 in adult patients with FA. Design plans to dose at least three cohorts and expects to report initial data from the MAD trial in mid-2023 with final data expected by year-end.

Fuchs Endothelial Corneal Dystrophy (FECD)

Disease Overview, Prevalence and Current Treatment Landscape

FECD is a genetic eye disease characterized by bilateral degeneration of corneal endothelial cells (CECs) and progressive loss of vision. Typically, the disease manifests after age 40 and can be detected through routine eye exam. As individuals age, CECs become dysfunctional and degenerate and eventually fluid accumulates in the cornea (corneal edema). As disease progresses, FECD leads to reduced visual acuity, reduced contrast sensitivity, glare, and can eventually lead to corneal blindness. Other symptoms include pain and grittiness in the eye.

This genetic eye disease affects millions of people worldwide. Over 70% of FECD cases are caused by cytosine-thymine-guanine (CTG) nucleotide repeat expansions in the TCF4 gene, which is transcribed into pathogenic TCF4 RNA that forms nuclear foci and sequesters splicing proteins, leading to transcript mis-splicing (spliceopathy) and loss of CECs. CECs harbor the longest known TCF4 repeat expansions in the body, potentially explaining why the cornea is the only affected tissue. There is currently no effective therapeutic intervention that addresses the root cause of the disease. Various modalities of keratoplasty, including corneal transplantation, constitute the only treatment option to correct advanced FECD.

Our Approach

Our FECD program leverages our expertise in designing GeneTAC™ small molecules to address the underlying cause of the disease. FECD GeneTAC™ molecules we designed have been shown to markedly reduce nuclear foci and improve spliceopathy in FECD CEC cultures derived from the corneal tissue of donors who ultimately underwent corneal transplant.

In December 2022, we nominated DT-168 as a development candidate for FECD. DT-168 is a GeneTAC™ small molecule designed to target the CTG repeats in the TCF4 gene and selectively block transcription of the expansion-containing allele. DT-168 is currently the only therapeutic development program designed to address the genetic root cause of FECD while benefiting from the favorable development advantages of small molecules, including that it is designed to be applied as an eye drop. We are currently conducting IND-enabling studies to support continued development of DT-168.

Preclinical Data

In preclinical studies in FECD patient CECs that contained toxic nuclear TCF4 RNA, we observed reduction of pathogenic nuclear foci following exposure to our FECD GeneTAC™ molecules. As illustrated in Figure 7, we observed a reduction in CTG nuclear foci in FECD patient CECs exposed to our FECD GeneTAC™ molecules as determined through a fluorescence in situ hybridization imaging and analysis. This reduction was seen within several days after exposure to our FECD GeneTAC™ molecules at therapeutically relevant concentrations (IC50<10 nM).

With suppression of the mutant TCF4 transcription, reduction of formation of pathogenic nuclear foci and release of splicing proteins, the FECD GeneTAC™ molecules corrected aberrant splicing, thus allowing restoration of normal mRNA processing. As illustrated in Figure 8, FECD GeneTAC™ molecules reduced the abnormal MBNL1 RNA levels to that seen in healthy CECs at therapeutically relevant concentrations in CECs from multiple FECD patients.

We formulated DT-168 as an eye drop and showed that it was well-tolerated following 2 weeks of topical ocular dosing in rabbits and distributed throughout the cornea.

The findings to date support further development of DT-168 as a potential disease-modifying therapy. We plan to submit an IND for DT-168 in the second half of 2023.

Figure 7: FECD GeneTAC™ molecules reduced pathogenic TCF4 foci in CECs isolated from patients with FECD

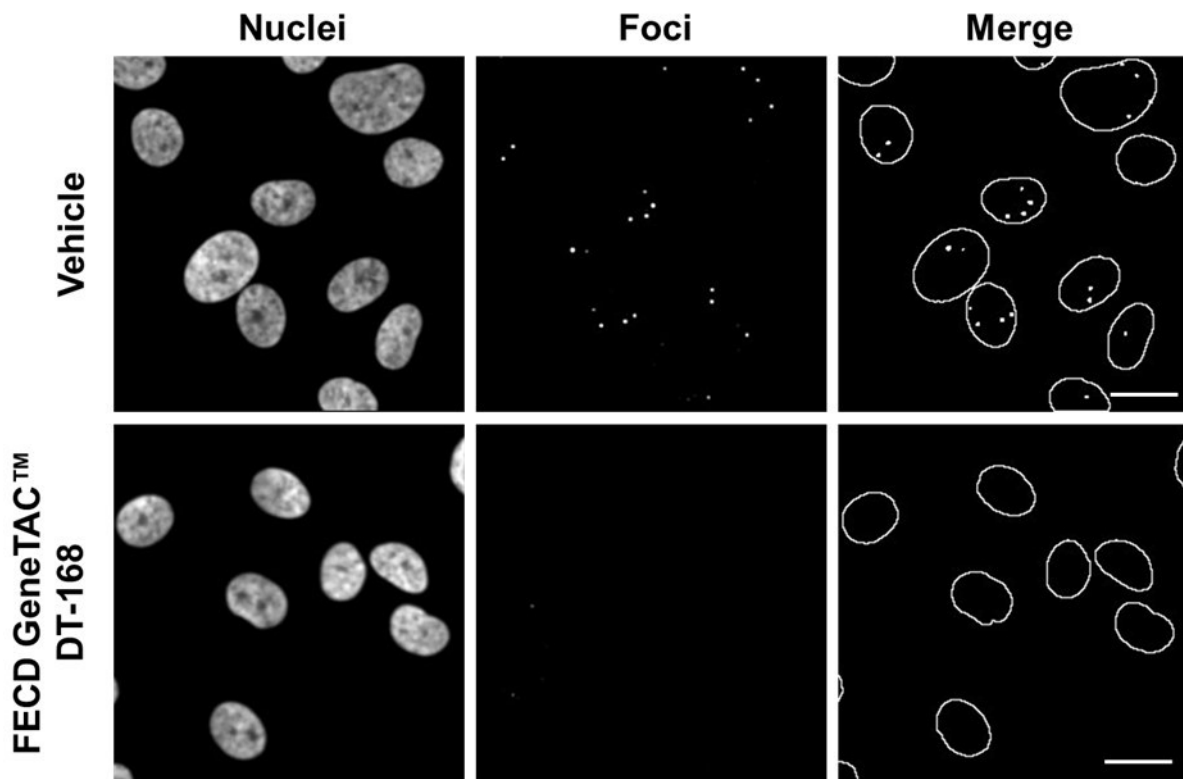
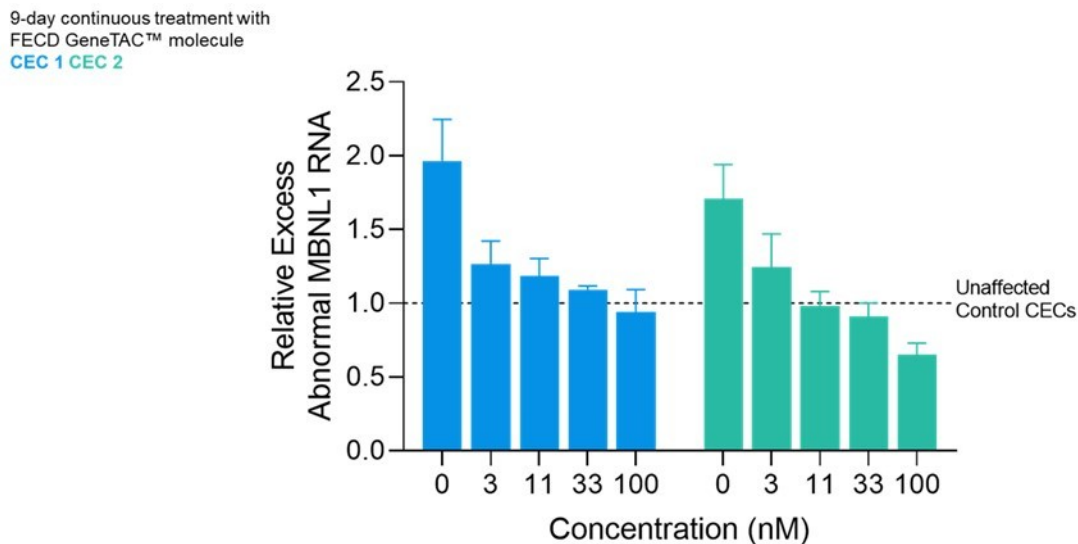


Figure 8: GeneTAC™ molecules corrected aberrant splicing events in CECs isolated from patients with FECD



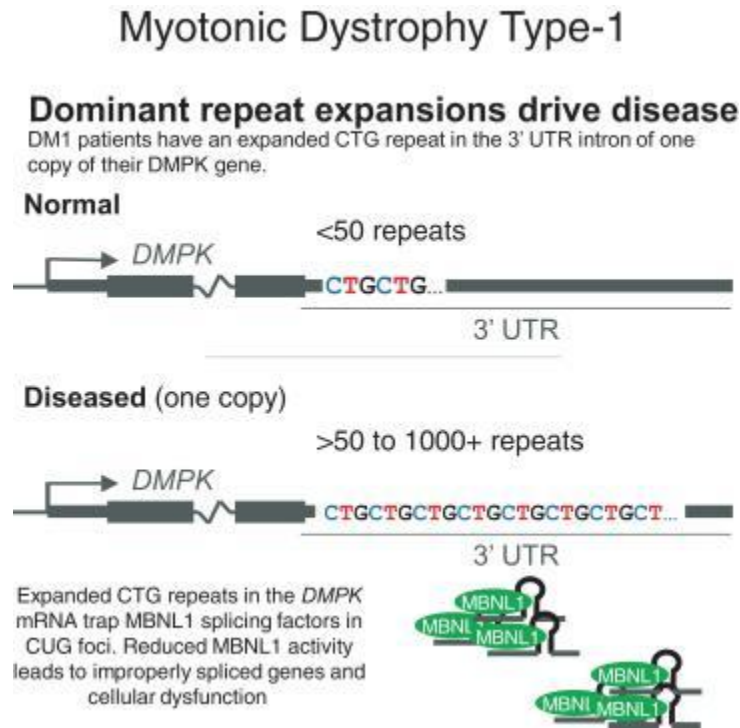
Myotonic Dystrophy Type-1 (DM1)

Disease Overview, Prevalence and Current Treatment Landscape

DM1 is a dominantly-inherited, monogenic progressive neuromuscular disease affecting skeletal muscle, heart, brain, and other organs. Clinical manifestations include muscle weakness, myotonia (slow muscle relaxation), early cataracts, cardiac arrhythmias and changes in neuropsychological function. DM1 is progressive and may become extremely disabling, leading to poor quality of life and early mortality.

DM1 is caused by a mutation that leads to an increased number of CTG triplet repeats found in the 3' non-coding region of the DMPK gene (Figure 9). The number of repeats ranges from up to approximately 35 in healthy individuals to many thousands in DM1 patients. When transcribed, the higher-than-normal number of triplet repeats in terminal end of the mutant DMPK allele form pre-mRNAs with large CUG hairpin loops that remain entrapped in the nucleus and form clumps also called foci. Specifically, mutant DMPK pre-mRNA sequesters a critical CUG-binding protein, muscle blind-like protein 1 (MBNL1), which leads to the formation of pathogenic nuclear foci and inhibits the ability of MBNL1 in processing many pre-mRNAs. As a result, multiple pre-mRNAs that encode key proteins are mis-spliced. This mis-splicing in the nucleus results in the translation of atypical proteins, which ultimately cause the clinical presentation of DM1. When levels of mutant DMPK mRNA containing higher numbers of CUG repeats are reduced, nuclear foci are diminished and MBNL1 proteins are freed to function normally. This disease process is illustrated below:

Figure 9: DM1: Genetic basis and clinical presentation



DM1 is estimated to have a genetic prevalence of 1 in 2,300-8,000 people, affecting more than 70,000 people in the United States and more than 90,000 people in Europe. However, we believe that the patient population is currently underdiagnosed due to lack of available therapies. DM1 is typically categorized into four overlapping phenotypes based on age of onset: late-onset; classical (adult-onset); childhood; and congenital (cDM1).

Overview of DM1 phenotypes

Phenotype	Age of onset	Estimated % of DM1 patients
Late-onset	40+ years	~10%
Classical (Adult-onset)	10 – 40 years	~65% to 75%
Childhood	1 - 10 years	~15%
Congenital (cDM1)	Birth	~5% to 15%

All DM1 phenotypes, except the late-onset form, are associated with high levels of disease burden and premature mortality. The clinical course of DM1 is progressive, and may become extremely disabling, especially when more generalized limb weakness and respiratory muscle involvement develops. Systemic manifestations such as fatigue, GI complications, cataracts and excessive daytime sleepiness greatly impact a patient’s quality of life. As a result, DM1 leads to physical impairment, activity limitations, decreased participation in social activities and work and impairs quality of life for patients and their families. Life expectancy in classical DM1 ranges from 48-55 years. Respiratory failure due to muscle weakness (especially diaphragmatic weakness) causes at least 50% of early mortality, and cardiac abnormalities, including sudden death, account for approximately 30% of early mortality.

There are currently no approved therapies for the treatment of DM1, leaving a high unmet medical need and opportunity for new disease-modifying therapies. There are several product candidates currently in preclinical and clinical development, one of which is in later stage clinical development and does not show disease-modifying potential, while the other product candidates are in preclinical stages and have yet to demonstrate clinical proof-of-concept.

Our Approach

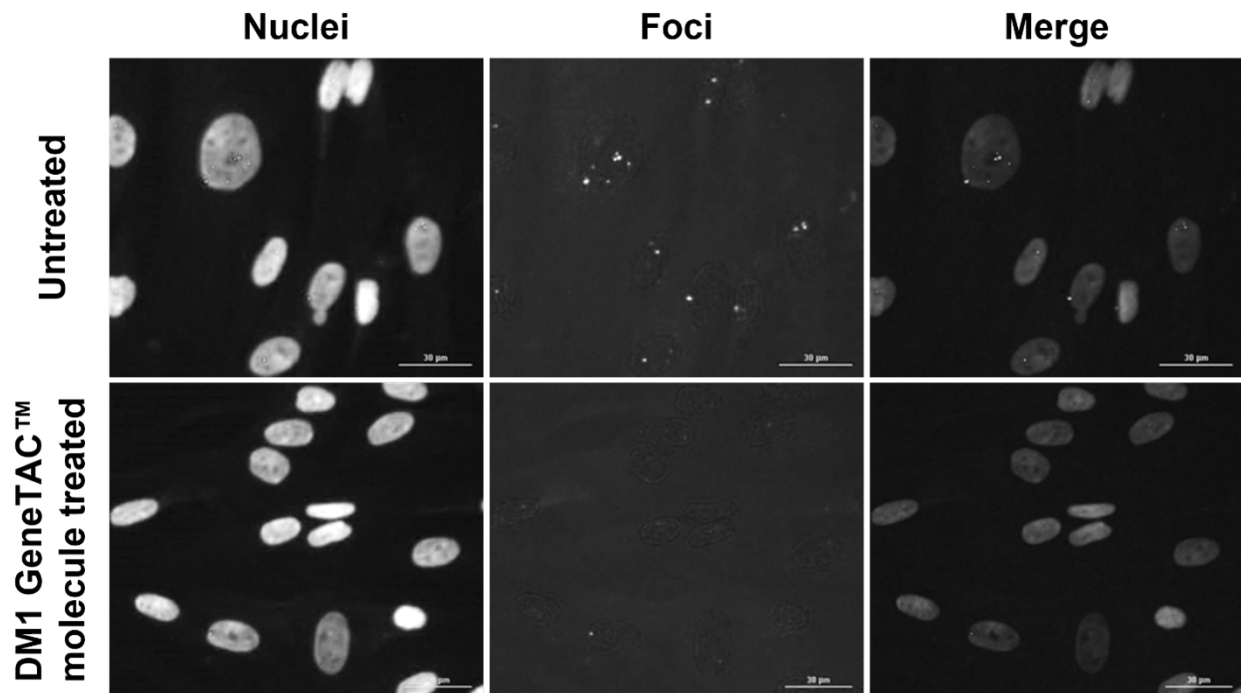
Our DM1 program is based on GeneTAC™ small molecule candidates consisting of a DNA-targeting moiety designed to target to the CTG repeats in the 3' untranslated region of the DMPK gene, linked to a ligand moiety that is designed to block transcription of the mutant expanded CTG repeat without disrupting the normal DMPK expression. As a result, the DM1 GeneTAC™ molecule is designed to prevent the formation of the CUG hairpin structures that trap splicing proteins and produce nuclear foci. Like our FA program, the DM1 program is designed to address the underlying cause of the disease and benefit from the favorable development advantages of small molecules.

Preclinical Data

We are currently conducting preclinical studies of our DM1 GeneTAC™ molecules in DM1 patient cells. We have observed reduced nuclear foci in DM1 cells from multiple patients after administration of our DM1 GeneTAC™ molecules. We believe these data support the potential for our DM1 GeneTAC™ molecules to be evaluated in clinical trials as a potential therapy for patients with DM1.

In preclinical studies in DM1 patient cells that contained toxic nuclear DMPK RNA, we observed reduction of nuclear foci following exposure to our DM1 GeneTAC™ molecules. When toxic nuclear DMPK levels are reduced, the nuclear foci are diminished, releasing splicing proteins, allowing restoration of normal mRNA processing, and potentially stopping or reversing disease progression. As illustrated in Figure 10, we observed a reduction in CUG nuclear foci in DM1 patient cells exposed to our DM1 GeneTAC™ molecules as determined through a fluorescence in situ hybridization imaging and analysis. This reduction was seen within several days after exposure to our DM1 GeneTAC™ molecules. The reduced CUG nuclear foci are indicated by the reduction in green punctate staining.

Figure 10: Decrease in CUG nuclear foci in DM1 patient cells exposed to DM1 GeneTAC™ molecules



In preclinical studies in cells from multiple DM1 patients, we observed a reduction in the number of observable CUG nuclear foci after exposure to our DM1 GeneTAC™ molecule. As seen in Figure 11, after exposing DM1 Patient 1 and 2 cells to our DM1 GeneTAC™ molecules, we observed an increase in the percentage of cells with no observable CUG nuclear foci to over 92%, similar to healthy cells.

Figure 11: CUG nuclear foci in cells from multiple DM1 patients

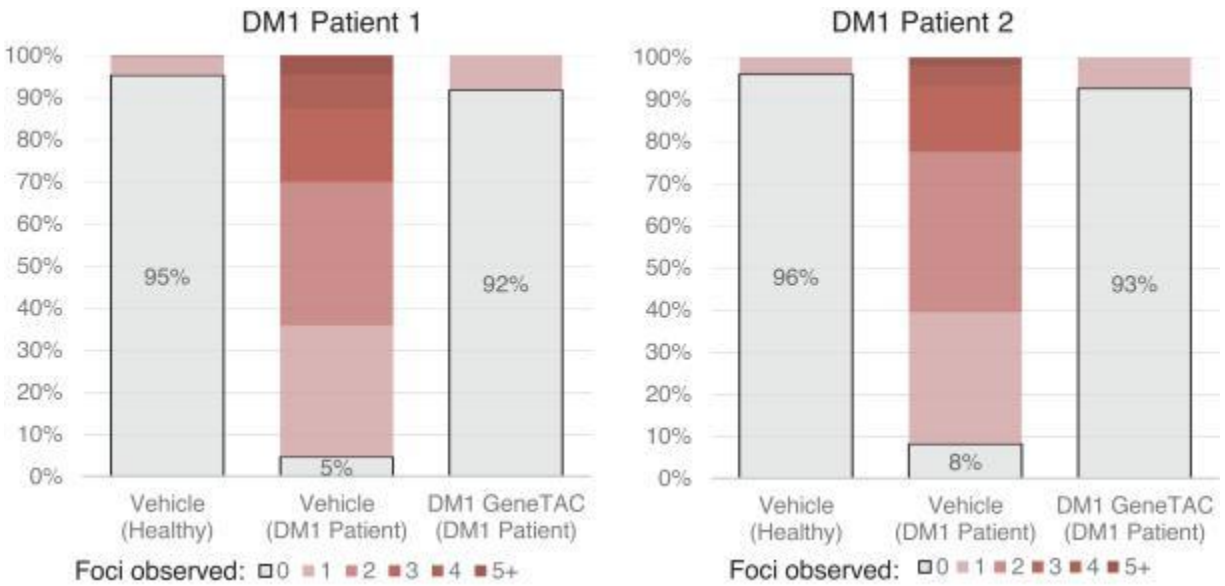
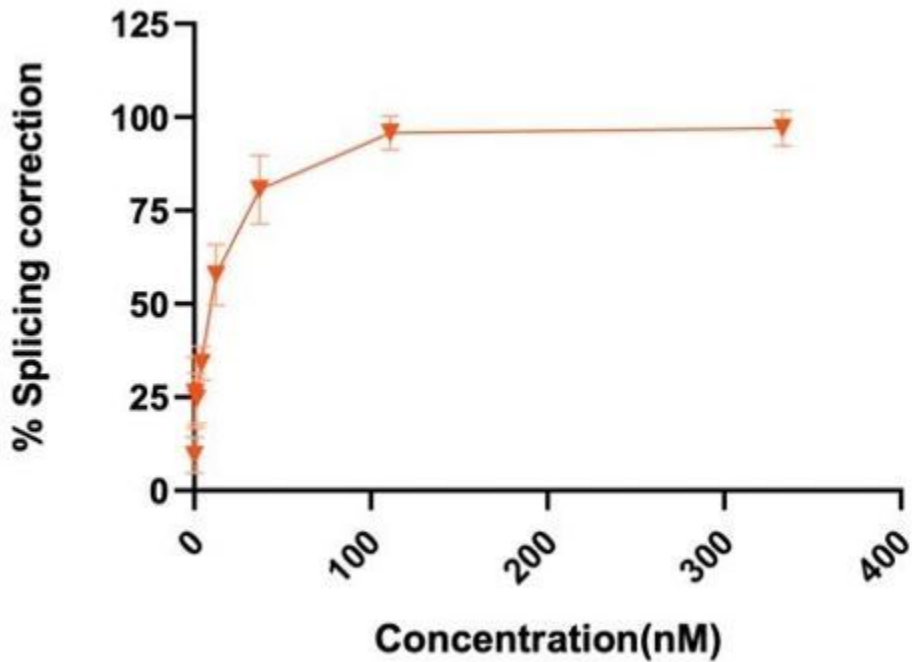


Figure 12: Percent splicing correction for MBNL1 exon 7 inclusion in DM1 patient fibroblasts



DM1 GeneTAC™ molecules corrected splicing defects in MBNL-1 transcript in DM1 myoblasts and restored the splicing levels to >90% of that seen in healthy human skeletal myoblasts (Figure 12). We plan to continue evaluating the properties of our DM1 GeneTAC™ molecules in both *in vivo* and *in vitro* preclinical studies. We expect to complete IND-enabling studies and submit an IND in 2024.

Discovery Programs

We are also advancing our GeneTAC™ portfolio in other serious nucleotide repeat expansion-driven monogenic diseases, such as fragile X syndrome, spinocerebellar ataxias, Huntington disease, spinobulbar muscular atrophy and C9orf72-amyotrophic lateral sclerosis/frontotemporal dementia as outlined in the table below. Many of these monogenic diseases have overlapping triplet repeat expansions, including CTG repeats that cause DMI, allowing for the accumulating knowledge on how to design novel molecules to be applied across multiple diseases, also caused by CTG and CAG repeat expansions. Additionally, our medicinal chemistry experiences with GeneTAC™ molecules allow us to more rapidly design GeneTAC™ molecules for additional indications.

Figure 13: Potential broad applicability of GeneTAC™ molecules across multiple indications

RESEARCH PROGRAMS	ESTIMATED US PREVALENCE
Fragile X syndrome (FXS; CGG)	~80,000
Huntington disease (HD; CAG)	~40,000
C9orf72-amyotrophic lateral sclerosis/ frontotemporal dementia (ALS/FTD; GGGGCC)	~7,000
Other CTG-expansion diseases	~25,000

Competition

The biotechnology and biopharmaceutical industries are characterized by rapid technological advancement, significant competition and an emphasis on intellectual property. Any product candidates that we successfully design, develop and commercialize will compete with current therapies and new therapies that may become available in the future. While we believe that our technology, development experience and scientific knowledge in the field of nucleotide repeat expansion diseases and small molecules, and foundational intellectual property provide us with competitive advantages, we face potential competition from many different sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions and governmental agencies and public and private research institutions.

Friedreich Ataxia. On February 28, 2023, Reata Pharmaceuticals announced that the FDA approved omaveloxolone, a Nrf2 activator, for the treatment of FA in adults and adolescents aged 16 years and older. We are also aware of a number of companies with active clinical stage FA programs including (i) Larimar Therapeutics evaluating CTI-1601, a cell penetrating peptide FXN recombinant fusion protein, (ii) Lexeo Therapeutics evaluating a cardiac targeted FXN gene therapy, (iii) Minoryx Therapeutics evaluating leriglitazone, a PPAR-gamma agonist, and (iv) PTC Therapeutics evaluating vatiquinone, a 15-lipoxygenase inhibitor. In addition, several companies have stated that they have gene therapy programs for FA including Lacerta Therapeutics, Novartis, Pfizer, PTC Therapeutics, Solid Biosciences, StrideBio, and Voyager Therapeutics.

Fuchs Endothelial Corneal Dystrophy. We are aware of a number of companies with active clinical stage FECD programs including (i) Aurion Biotech evaluating Vyznova, expanded donor cells for transplant, (ii) Emmecell evaluating donor cornea endothelial cells delivered through magnetic nanoparticles injected into the anterior chamber, (iii) Kowa Pharmaceutical evaluating Ripasudil, a Rho-kinase inhibitor, for use in conjunction with corneal surgery, (iv) Santen Pharmaceutical evaluating STN1010904, an mTOR inhibitor, and (v) Trefoil Therapeutics evaluating TTHX1114, an engineered FGF1 delivered via intracameral injection, for use in conjunction with corneal surgery.

Myotonic Dystrophy Type-1. We are aware of a number of programs for DM1 including (i) AMO Pharma evaluating tideglusib, a GSK3-β inhibitor, (ii) small molecules interacting with RNA under evaluation by Anima Biotech, (iii) anti-miRNA oligonucleotides under evaluation by Arthex Biotech, (iv) Astellas Pharma evaluating an AAV-antisense candidate, (v) Avidity Biosciences evaluating an antibody linked siRNA, (vi) Dyne Therapeutics evaluating an antibody linked oligonucleotide, (vii) Entrada Therapeutics evaluating a peptide conjugated oligonucleotide, (viii) an AAV-based RNA degrading gene therapy by Enzerna Biosciences, (ix) small molecules interacting with RNA under evaluation by Expansion Therapeutics, (x) Harmony Biosciences evaluating a histamine 3 receptor for the treatment of excessive daytime sleepiness in DM1, (xi) an RNA-targeting AAV-based gene therapy by Locanabio, (xii) PepGen evaluating a peptide conjugated antisense oligonucleotide, and (xiii) gene editing treatments by Vertex Pharmaceuticals.

Other Nucleotide Repeat Expansion Driven Diseases. There are currently no approved therapies targeting the underlying cause of other inherited nucleotide repeat expansion diseases where we believe GeneTAC™ molecules could have applicability, including fragile X syndrome, spinocerebellar ataxias, Huntington disease, spinobulbar muscular atrophy and C9orf72-amyotrophic lateral sclerosis/frontotemporal dementia, among others.

We will also compete more generally with other companies developing product candidates that utilize alternative scientific and technological approaches to modulate individual genes, including other companies working to develop nuclease-based gene editing technologies, such as Beam Therapeutics, CRISPR Therapeutics, Editas Medicine, Intellia Therapeutics, Precision BioSciences and Sangamo Biosciences.

Many of our competitors, either alone or with strategic partners, have substantially greater financial, technical and human resources 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. Merger and acquisition activity in the biotechnology and biopharmaceutical industries may result in even more resources being concentrated within a smaller number of our competitors. These companies also compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials and acquiring technologies complementary to, or necessary for, our programs. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. Our commercial opportunity could be substantially limited if our competitors develop and commercialize products that are more effective, safer, less toxic, more convenient or less expensive than our comparable products. In geographies that are critical to our commercial success, competitors may also obtain regulatory approvals before us, resulting in our competitors building a strong market position in advance of the entry of our products. In addition, our ability to compete may be affected in many cases by insurers or other third-party payors seeking to encourage the use of other drugs. The key competitive factors affecting the success of our programs are likely to be their efficacy, safety profile, biodistribution, manufacturability, effectiveness of commercial activities, intellectual property protection and availability of reimbursement.

License Agreement

License Agreement with Wisconsin Alumni Research Foundation

On February 20, 2019, we and Wisconsin Alumni Research Foundation (WARF) entered into a human therapeutics exclusive license agreement (the WARF License Agreement), pursuant to which we received (i) an exclusive, worldwide, royalty-bearing, sublicensable license under certain of WARF's patents relating to compounds and methods for treating genetic disease by modulating gene expression, including expression of frataxin, through nucleic acid binding moieties that specifically bind to one or more repeats of a target oligonucleotide sequence as well as a synthetic transcription factor having a nucleic acid binding moiety that specifically binds to a target oligonucleotide sequence and (ii) a non-exclusive, worldwide, sublicensable license under certain of WARF's know-how relating to the foregoing patents, in each case (i) and (ii), to research, develop, make, have made, use, have used, sell, offer for sale, have sold, export and import products developed through the use of such licensed patents and know-how in all fields. We are currently using the licensed patents and know-how in our FA program. The licenses granted pursuant to the WARF License Agreement are subject to certain rights retained by (i) the United States government under the Bayh-Dole Act and (ii) WARF to grant the University of Wisconsin, non-profit research institutions collaborating with the University of Wisconsin and governmental agencies non-exclusive licenses to practice and use the licensed patents for non-commercial research purposes. Such rights retained by the United States government and WARF are typical for a license from a U.S. university or research institution, and we believe such rights do not pose a material risk to our business. We further granted to WARF, the University of Wisconsin, the inventors of the licensed patents, and governmental research organizations a covenant not to sue under certain improvements to the licensed patents for non-commercial research purposes. Under the WARF License Agreement, we are required to use commercially reasonable diligence to develop, seek regulatory approval for, manufacture, market and sell licensed products throughout the term of the agreement, including satisfying certain funding and diligence milestones.

In consideration for the rights granted to us under the WARF License Agreement, we paid WARF an upfront licensing fee of \$250,000 and a milestone fee of \$125,000 following the submission of our IND for DT-216. We are also required to pay WARF up to an aggregate of \$17.5 million upon the achievement of certain development and commercial sales milestones. Each such milestone payment is payable once for each licensed product for which the milestone is achieved, except for the two milestones relating to IND submission and human proof of concept study, which are payable only for the first licensed product for which such milestones are achieved (and not for subsequent licensed products). In addition, we are required to pay WARF, on a licensed product-by-licensed product and country-by-country basis, upon first commercial product sale, a fixed royalty of a low single digit percentage on sales of licensed products by us and/or by our sublicensees, subject to certain reductions and a minimum total annual royalty payment of \$100,000. Our royalty obligation will terminate on the date of expiration of the last-to-expire of the licensed patents in the relevant country. We are also obligated to pay WARF sublicense fees in the mid-single digits percentage for funding or royalties earned from the granting of sublicenses to the WARF patents and know-how. We are required to reimburse WARF for all costs associated with filing, prosecuting and maintaining the licensed patents prior to and after the effective date of the WARF License Agreement.

The WARF License Agreement will continue until the earliest of (i) the date of early termination in accordance with the agreement, (ii) expiration of the licensed patents in all countries, or (iii) our cessation, once begun, of royalty payments for more than two years. The WARF License Agreement may be terminated by us upon 90 days' written notice, provided we include a statement of reasons for termination. WARF may terminate the WARF License Agreement (a) upon written notice if our cumulative earned royalties paid to WARF does not exceed \$0.1 million on or before December 31, 2031, (b) if we fail to make timely payments, fail to timely provide development reports or provide any false information with respect thereto, fail to actively pursue the development plan, or commit any breach of any other covenant, representation or warranty under the WARF License Agreement, in each case, without curing such failure or breach within 90 days after written notice thereof, (c) if we commit any act of bankruptcy or become insolvent, or (d) immediately if we or our sublicensee(s) offer any rights to the licensed patents to our or our sublicensees' creditors. As of December 31, 2022, the licensed patents include one issued U.S. patent that is projected to expire on or around March 29, 2037, not including any patent term adjustments and extensions. The license also includes seven pending patent applications in the United States, Europe, Canada, and Australia. Any patents that issue from these patent applications have projected expiration dates from 2037 through 2039, not including any patent term adjustments and extensions that may be available.

Manufacturing

GeneTAC™ molecules are synthetically tractable, offering a readily scalable, cost-effective development path that does not require complex customized equipment and processes. We do not own or operate, and currently have no plans to establish, current Good Manufacturing Practice (cGMP) manufacturing facilities and laboratories. We currently rely on third-party manufacturers and suppliers for the raw materials and starting components used to make our GeneTAC™ molecules, and we expect to continue to do so to meet our research and development and commercial activities. Our third-party manufacturers are qualified to manufacture our product candidates under cGMP requirements and other applicable laws, guidances and regulations. We believe there are multiple sources for all of the materials and components required for the manufacture of our product candidates.

Intellectual Property

Our success depends in part on our ability to obtain and maintain proprietary protection for our product candidates and other discoveries, inventions, trade secrets and know-how that are critical to our business operations. Our success also depends in part on our ability to operate without infringing the proprietary rights of others, and in part, on our ability to prevent others from infringing our proprietary rights. A comprehensive discussion on risks relating to intellectual property is provided under the heading “Risk Factors” under Part I, Item 1A of this Annual Report.

As of December 31, 2022, we own 19 pending U.S. patent applications, eight pending European patent applications, two pending patent applications in Argentina, two pending patent applications in Taiwan, a pending patent application in Canada, China, and Japan, respectively, and three pending Patent Cooperation Treaty applications, which, if issued (or in case of provisional applications, if issued from future non-provisional applications that we file), are expected to expire between 2039 and 2043, not including any patent term adjustments and extensions that may be available. In addition, we acquired an exclusive license from WARF under one issued U.S. patent, three pending U.S. patent applications, one pending European patent application, two pending Canadian patent applications and one pending Australian patent application, with the issued patent expected to expire in 2037 and the other patents, if issued, are expected to expire between 2037 and 2039, not including any patent term adjustments and extensions that may be available. These patents cover our proprietary GeneTAC™ Platform technology that is used in our FA program, DM1 program and other therapeutic programs directed to genetic diseases that are further discussed below.

For our FA program, as of December 31, 2022, we own or hold an exclusive, worldwide license from WARF. In particular, we have licensed from WARF an issued U.S. patent, a pending U.S. patent application, and a pending patent application in Europe and Canada, respectively, directed to compounds and methods for modulating frataxin expression and treatment of FA. The U.S. patent and any patents issued from these pending patent applications are projected to expire on or around March 29, 2037, not including any patent term adjustments and extensions. We also license from WARF one pending U.S. patent application and two pending patent applications in Australia and Canada directed to methods and other compounds for treatment of FA. Any patents that eventually issue from this patent application are projected to expire on or around October 22, 2039, not including any patent term adjustments and extensions that may be available. Additionally, we own nine pending U.S. patent applications, two pending patent applications in Europe, Argentina and Taiwan, respectively, a pending patent application in Canada, China, and Japan, respectively, and a pending Patent Cooperation Treaty application directed to other compositions of matter and methods for the treatment of FA. Any patents that eventually issue from these patent applications are projected to expire in the 2039-2043 timeframe, not including any patent term adjustments and extensions that may be available.

For our FECD program, as of December 31, 2022, we own three U.S. patent applications, a pending patent application in Europe, and a pending Patent Cooperation Treaty application directed to compositions of matter and methods for the treatment of FECD. Any patents issuing from these patent applications are projected to expire in 2043, not including any patent term adjustments and extensions that may be available.

For our DM1 program, as of December 31, 2022, two of our pending U.S. patent applications, one pending patent application in Europe, and one pending Patent Cooperation Treaty application are directed to compositions of matter and methods for the treatment of DM1. Any patents issuing from patent applications in these families are projected to expire in the 2039-2043 timeframe, not including any patent term adjustments and extensions that may be available.

As of December 31, 2022, nine of our pending U.S. patent applications, seven of our pending patent applications in Europe and a pending Patent Cooperation Treaty application are directed to our therapeutic programs related to other genetic diseases (including, but not limited to, fragile X syndrome, spinocerebellar ataxias, Huntington disease, spinobulbar muscular atrophy, and C9orf72-amyotrophic lateral sclerosis/frontotemporal dementia) and the development of potential disease-modifying compounds. These therapeutic programs and the development of potential disease-modifying compounds utilize our GeneTAC™ Platform technology and any patents that issue from these patent applications are projected to expire in the 2039-2043 timeframe not including any patent term adjustments or extensions. We also license from WARF a pending U.S. patent application that, if issued, is projected to expire on or around March 29, 2038, not including any patent term adjustments or extensions. These patent applications cover compositions of matter and methods of treating the related genetic diseases under our therapeutic programs, including the use of transcription modulator molecules that contain a DNA-binding moiety capable of specifically binding to certain nucleotide repeat sequences that are implicated in the applicable genetic disease. In addition to patent protection, we rely on trade secret protection, trademark protection and know-how to expand our proprietary position around our chemistry, technology and other discoveries and inventions that we consider important to our business. We are a party to the WARF License Agreement, described in more detail above, under which we are granted intellectual property rights to know-how that are important to our business.

We also seek to protect our intellectual property by having confidentiality terms in our agreements with companies with whom we share proprietary and confidential information in the course of business discussions, and by having confidentiality terms in our agreements with our employees, consultants, scientific advisors, clinical investigators and other contractors and also by requiring our employees, commercial contractors, and certain consultants and investigators, to enter into invention assignment agreements that grant us ownership of any discoveries or inventions made by them while in our employ.

Government Regulation and Product Approval

As a pharmaceutical company that operates in the United States, we are subject to extensive regulation. Government authorities in the United States (at the federal, state and local level) and in other countries extensively regulate, among other things, the research, development, testing, manufacturing, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, post-approval monitoring and reporting, marketing and export and import of drug products such as those we are developing. Product candidates that we develop must be approved by the Food and Drug Administration (FDA), before they may be legally marketed in the United States and by the appropriate foreign regulatory agency before they may be legally marketed in foreign countries. Generally, our activities in other countries will be subject to regulation that is similar in nature and scope as that imposed in the United States, although there can be important differences. Additionally, some significant aspects of regulation in Europe are addressed in a centralized way, but country-specific regulation remains essential in many respects.

U.S. Drug Development Process

In the United States, the FDA regulates drugs under the Federal Food, Drug and Cosmetic Act (FDCA), and implementing regulations. A new drug must be approved by the FDA through the new drug application (NDA) process before it may be legally marketed in the United States. Drugs are also subject to other federal, state and local statutes and regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources. 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 administrative or judicial sanctions. FDA sanctions could include, among other actions, refusal to approve pending applications, withdrawal of an approval, a clinical hold, warning letters, product recalls or withdrawals from the market, product seizures, total or partial suspension of production or distribution injunctions, fines, refusals of government contracts, restitution, disgorgement or civil or criminal penalties. Any agency or judicial enforcement action could have a material adverse effect on us. The process required by the FDA before a drug may be marketed in the United States generally involves the following:

- completion of extensive preclinical laboratory tests, preclinical animal studies and formulation studies in accordance with applicable regulations, including the FDA's Good Laboratory Practice (GLP) regulations and other applicable regulations;
- submission to the FDA of an IND, which must become effective before human clinical trials may begin;
- approval by an independent institutional review board (IRB) at each clinical site before each trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with applicable regulations, including the FDA's good clinical practice (GCP) regulations to establish the safety and efficacy of the proposed drug for its proposed indication;
- submission to the FDA of an NDA after completion of all pivotal trials;
- a determination by the FDA within 60 days of its receipt of an NDA to file the NDA for review;
- satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities where the drug is produced to assess compliance with the FDA's cGMP requirements to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity;
- potential FDA audit of the preclinical and/or clinical trial sites that generated the data in support of the NDA to assess compliance with GCP regulations;
- satisfactory completion of an FDA advisory committee review, if applicable; and
- FDA review and approval of the NDA prior to any commercial marketing or sale of the drug in the United States.

Before testing any compounds with potential therapeutic value in humans, the product candidate enters the preclinical testing stage. Preclinical tests include laboratory evaluations of product chemistry, toxicity and formulation, as well as animal studies, to assess the potential safety and activity of the product candidate. The conduct of the preclinical tests must comply with federal regulations and requirements including GLP requirements. The sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and a proposed clinical protocol, to the FDA as part of the IND. An IND is a request for authorization from the FDA to administer an investigational drug product to humans. The central focus of an IND submission is on the general investigational plan and the protocol(s) for human trials. Some preclinical testing may continue even after the IND is submitted. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA raises concerns or questions regarding the proposed clinical trials and places the IND on clinical hold within that 30-day time period. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. The FDA may also impose clinical holds on a product candidate at any time before or during clinical trials due to safety concerns or non-compliance.

Clinical trials involve the administration of the product candidate to healthy volunteers or patients under the supervision of qualified investigators, generally physicians not employed by or under the trial sponsor's control, in accordance with GCPs, which include the requirement that all research subjects provide their informed consent for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria and the parameters to be used to monitor subject safety and assess efficacy. Each protocol, and any subsequent amendments to the protocol, must be submitted to the FDA as part of the IND. Further, each clinical trial must be reviewed and approved by an independent IRB at or servicing each institution at which the clinical trial will be conducted. 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 approves 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 completed. There are also requirements governing the reporting of ongoing clinical trials and completed clinical trial results to public registries.

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

- **Phase 1.** The drug is initially introduced into healthy human subjects and tested for safety, dosage tolerance, absorption, metabolism, distribution and excretion, the side effects associated with increasing doses and if possible, to gain early evidence of effectiveness. In the case of some products for severe or life-threatening diseases, especially when the product may be too inherently toxic to ethically administer to healthy volunteers, the initial human testing is often conducted in patients.
- **Phase 2.** The drug is evaluated in a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases or conditions and to determine dosage tolerance, optimal dosage and dosing schedule. Multiple Phase 2 clinical trials may be conducted to obtain information prior to beginning larger and more expensive Phase 3 clinical trials.
- **Phase 3.** The drug is administered to an expanded patient population to further evaluate dosage and clinical efficacy at geographically dispersed clinical trial sites. These clinical trials are intended to establish the overall benefit/risk ratio of the product and provide an adequate basis for product approval. Generally, two adequate and well-controlled Phase 3 clinical trials are required by the FDA for approval of an NDA.

Post-approval studies, or 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, FDA may mandate the performance of Phase 4 trials. In certain instances, the FDA may mandate the performance of Phase 4 clinical trials as a condition of approval of an NDA.

During the development of a new drug, sponsors are given opportunities to meet with the FDA at certain points. These points may be prior to submission of an IND, at the end of Phase 2, and before an NDA is submitted. Meetings at other times may be requested. These meetings can provide an opportunity for the sponsor to share information about the data gathered to date, for the FDA to provide advice, and for the sponsor and the FDA to reach agreement on the next phase of development. Sponsors typically use the meetings at the end of the Phase 2 trial to discuss Phase 2 clinical results and present plans for the pivotal Phase 3 clinical trials that they believe will support approval of the new drug.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and written IND safety reports must be submitted to the FDA and the investigators for serious and unexpected AEs or any finding from tests in laboratory animals that suggests a significant risk for human subjects. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, if at all. The FDA, the IRB, or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients. Additionally, some clinical trials are overseen by an independent group of qualified experts organized by the clinical trial sponsor, known as a data safety monitoring board or committee. This group provides authorization for whether or not a trial may move forward at designated check points based on access to certain data from the trial.

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

U.S. Review and Approval Processes

Assuming successful completion of all required testing in accordance with all applicable regulatory requirements, the results of product development, preclinical studies and clinical trials, along with descriptions of the manufacturing process, analytical tests conducted on the chemistry of the drug, proposed labeling and other relevant information are submitted to the FDA as part of an NDA requesting approval to market the product. 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 to the satisfaction of the FDA. The submission of an NDA is subject to the payment of substantial user fees; a waiver of such fees may be obtained under certain limited circumstances.

In addition, the Pediatric Research Equity Act (PREA) requires a sponsor to conduct pediatric clinical trials for most drugs, for a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration. Under PREA, original NDAs and supplements must contain a pediatric assessment unless the sponsor has received a deferral or waiver. The required assessment must evaluate the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations and support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The sponsor or FDA may request a deferral of pediatric clinical trials for some or all of the pediatric subpopulations. A deferral may be granted for several reasons, including a finding that the drug is ready for approval for use in adults before pediatric clinical trials are complete or that additional safety or effectiveness data need to be collected before the pediatric clinical trials begin. The FDA must send a non-compliance letter to any sponsor that fails to submit the required assessment, keep a deferral current or fails to submit a request for approval of a pediatric formulation. Unless otherwise required by regulation, the Pediatric Research Equity Act does not apply to any drug for an indication for which orphan designation has been granted. However, if only one indication for a product has orphan designation, a pediatric assessment may still be required for any applications to market that same product for the non-orphan indication(s).

The FDA reviews all NDAs submitted before it accepts them for filing and may request additional information rather than accepting an NDA for filing. The FDA must make a decision on accepting an NDA for filing within 60 days of receipt. Once the submission is accepted for filing, the FDA begins an in-depth review of the NDA. Under the Prescription Drug User Fee Act (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. This review typically takes twelve months from the date the NDA is submitted to FDA because the FDA has approximately two months to make a “filing” decision after it the application is submitted. The FDA does not always meet its PDUFA goal dates for standard and priority NDAs, and the review process is often significantly extended by FDA requests for additional information or clarification.

After the NDA submission is accepted for filing, the FDA reviews the NDA to determine, among other things, whether the proposed product is safe and effective for its intended use and whether the product is being manufactured in accordance with cGMP to assure and preserve the product’s identity, strength, quality and purity. The FDA may refer applications for novel drug products or drug products which present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and 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 and typically follows the advisory committee’s recommendations.

Before approving an NDA, the FDA will inspect the facilities at which the product is manufactured. The FDA will not approve the product 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 sites to assure compliance with GCP requirements. After the FDA evaluates the application, manufacturing process and manufacturing facilities, it may issue an approval letter or a Complete Response Letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. 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 usually describes all of the specific deficiencies in the NDA identified by the FDA. The Complete Response Letter may require additional clinical data and/or (an) additional pivotal Phase 3 clinical trial(s), and/or other significant and time-consuming requirements related to clinical trials, preclinical studies or manufacturing. 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 if such data and information are submitted, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval.

If a product receives regulatory approval, the approval may be significantly limited to specific diseases and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the product. Further, the FDA may require that certain contraindications, warnings or precautions be included in the product labeling or may condition the approval of the NDA on other changes to the proposed labeling, development of adequate controls and specifications, or a commitment to conduct one or more post-market studies or clinical trials. For example, the FDA may require Phase 4 testing, which involves clinical trials designed to further assess a drug safety and effectiveness, and may require testing and surveillance programs to monitor the safety of approved products that have been commercialized. The FDA may also determine that a REMS is necessary to assure the safe use of the drug. 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 an approved REMS, if required. A REMS could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools.

Orphan Drug Designation

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug intended to treat a rare disease or condition, which is a disease or condition that affects fewer than 200,000 individuals in the United States or, if it affects more than 200,000 individuals in the United States, there is no reasonable expectation that the cost of developing and making a drug product available in the United States for this type of disease or condition will be recovered from sales of the product. Orphan designation must be requested before submitting an NDA. After the FDA grants orphan designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If a product that has orphan designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications to market the same drug or biological product for the same indication for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan exclusivity or inability to manufacture the product in sufficient quantities. The designation of such drug also entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers. Competitors, however, 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 product has exclusivity. If an orphan designated product receives marketing approval for an indication broader than what is designated, it may not be entitled to orphan exclusivity.

Expedited Development and Review Programs

The FDA has a number of programs intended to expedite the development or review of products that meet certain criteria. For example, the FDA has a fast track designation program that is intended to expedite or facilitate the process for reviewing new drug products that meet certain criteria. Specifically, new drugs are eligible for fast track designation if they are intended to treat a serious or life-threatening disease or condition and demonstrate the potential to address unmet medical needs for the disease or condition. Fast track designation applies to the combination of the product and the specific indication for which it is being studied. The sponsor of a fast track product has opportunities for more frequent interactions with the applicable FDA review team during product development and, once an NDA is submitted, the product candidate may be eligible for priority review. With regard to a fast track product, the FDA may consider for review sections of the NDA on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the NDA, the FDA agrees to accept sections of the NDA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the NDA.

Any product submitted to the FDA for approval, including a product with a fast track designation, may also be eligible for other types of FDA programs intended to expedite development and review, such as priority review and accelerated approval. A product is eligible for priority review if it is designed to treat a serious condition, and if approved, would provide a significant improvement in the treatment, diagnosis or prevention of a serious condition compared to marketed products. The FDA will attempt to direct additional resources to the evaluation of an application for a new drug designated for priority review in an effort to facilitate the review. The FDA endeavors to review applications with priority review designations within six months of the filing date as compared to ten months for review of new molecular entity NDAs under its current PDUFA review goals.

In addition, a product may be eligible for accelerated approval. Drug products intended to treat serious or life-threatening diseases or conditions may be eligible for accelerated approval upon a determination that the product has 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, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. As a condition of approval, the FDA may require that a sponsor of a drug receiving accelerated approval perform adequate and well-controlled post-marketing clinical trials to verify the predicted clinical benefit. Products receiving accelerated approval may be subject to expedited withdrawal procedures if the sponsor fails to conduct the required clinical trials, or if such trials fail to verify the predicted clinical benefit. In addition, the FDA currently requires as a condition for accelerated approval pre-approval of promotional materials, which could adversely impact the timing of the commercial launch of the product.

A sponsor may seek FDA designation of a product candidate as a “breakthrough therapy” if the drug 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. The designation includes intensive FDA interaction and guidance. If a drug is designated as breakthrough therapy, FDA will expedite the development and review of such drug. Breakthrough therapy designation includes all of the fast track program features, as well as more intensive FDA interaction and guidance. The breakthrough therapy designation is a distinct status from both accelerated approval and priority review, which can also be granted to the same drug if relevant criteria are met. If a product is designated as breakthrough therapy, the FDA will work to expedite the development and review of such drug.

Fast track designation, priority review, accelerated approval and breakthrough therapy designation do not change the standards for approval but may expedite the development or approval process. Even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened. In addition, such designations or shortened review periods may not provide a material commercial advantage.

Post-Approval Requirements

Any drug products manufactured or distributed pursuant to FDA approvals are subject to continuing regulation by the FDA, including, among other things, record-keeping requirements, reporting of adverse experiences with the product, providing the FDA with updated safety and efficacy information, product sampling and distribution requirements, and complying with FDA promotion and advertising requirements. After approval, most changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA review and approval. There also are continuing, annual program fees for any marketed products.

In addition, quality control and manufacturing procedures must continue to conform to applicable manufacturing requirements after approval to ensure the long term stability of the drug product. cGMP regulations require among other things, quality control and quality assurance as well as the corresponding maintenance of records and documentation and the obligation to investigate and correct any deviations from cGMP. Drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP and other laws. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance. In addition, changes to the manufacturing process are strictly regulated, and depending on the significance of the change, may require prior FDA approval before being implemented. Other types of changes to the approved product, such as adding new indications and additional labeling claims, are also subject to further FDA review and approval.

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

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters, or untitled letters;
- clinical holds on clinical studies;
- refusal of the FDA to approve pending applications or supplements to approved applications, or suspension or revocation 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;
- the issuance of safety alerts, Dear Healthcare Provider letters, press releases and other communications containing warnings or other safety information about the product; or
- injunctions or the imposition of civil or criminal penalties.

The FDA also may require post-marketing testing, known as Phase 4 testing, and surveillance to monitor the effects of an approved product. Discovery of previously unknown problems with a product or the failure to comply with applicable FDA requirements can have negative consequences, including adverse publicity, judicial or administrative enforcement, warning letters from the FDA, mandated corrective advertising or communications with doctors, and civil or criminal penalties, among others. Newly discovered or developed safety or effectiveness data may require changes to a product's approved labeling, including the addition of new warnings and contraindications, and also may require the implementation of other risk management measures.

The FDA closely regulates the marketing, labeling, advertising and promotion of drug products. A company can make only those claims relating to safety and efficacy, purity and potency that are approved by the FDA and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off label uses. Failure to comply with these requirements can result in, among other things, adverse publicity, warning letters, corrective advertising and potential civil and criminal penalties. Physicians may prescribe, 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 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 or 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.

In addition, the distribution of prescription pharmaceutical products is subject to the Prescription Drug Marketing Act, or PDMA, which regulates the distribution of drugs and drug samples at the federal level, and sets minimum standards for the registration and regulation of drug distributors by the states. Both the PDMA and state laws limit the distribution of prescription pharmaceutical product samples and impose requirements to ensure accountability in distribution.

Marketing Exclusivity

Market exclusivity provisions under the FDCA can also delay the submission or the approval of certain marketing applications. The FDCA provides a five-year period of non-patent marketing exclusivity within the United States to the first applicant to obtain 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 approve or even accept for review an abbreviated new drug application (ANDA) or a 505(b)(2) NDA submitted by another company for another drug based on the same active moiety, regardless of whether the drug is intended for the same indication as the original innovative drug or for another indication, where the applicant does not own or have a legal right of reference to all the data required for approval. However, an 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 alternatively provides three years of marketing exclusivity for an 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 covers only the modification for which the drug received approval on the basis of the new clinical investigations and does not prohibit the FDA from approving ANDAs for drugs containing the active agent for the original indication or condition of use. 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.

Orphan drug exclusivity, as described above, may offer a seven-year period of marketing exclusivity, except in certain circumstances. Pediatric exclusivity is another type of non-patent market exclusivity in the United States. Pediatric exclusivity, if granted, adds six months to existing exclusivity periods and patent terms. This six-month exclusivity, which runs from the end of other exclusivity protection or patent term, may be granted based on the voluntary completion of a pediatric trial in accordance with an FDA-issued "Written Request" for such a trial.

Other U.S. Healthcare Laws and Compliance Requirements

Although we currently do not have any products on the market, we are and, upon approval and commercialization, will be subject to additional healthcare regulation and enforcement by the federal government and by authorities in the states and foreign jurisdictions in which we conduct our business. In the United States, such laws include, without limitation, state and federal anti-kickback, fraud and abuse, false claims, privacy and security, price reporting, and physician sunshine laws and regulations.

The federal Anti-Kickback Statute prohibits, among other things, any person or entity, from knowingly and willfully offering, paying, soliciting or receiving any remuneration, directly or indirectly, overtly or covertly, in cash or in kind, to induce or in return for purchasing, leasing, ordering or arranging for the purchase, lease or order of any item or service reimbursable under Medicare, Medicaid or other federal healthcare programs. The term remuneration has been interpreted broadly to include anything of value. The Anti-Kickback Statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers, and formulary managers on the other. There are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution. The exceptions and safe harbors are drawn narrowly and practices that involve remuneration that may be alleged to be intended to induce prescribing, purchasing or recommending may be subject to scrutiny if they do not qualify for an exception or safe harbor. Failure to meet all of the requirements of a particular applicable statutory exception or regulatory safe harbor does not make the conduct per se illegal under the Anti-Kickback Statute. Instead, the legality of the arrangement will be evaluated on a case-by-case basis based on a cumulative review of all of its facts and circumstances. Our practices may not in all cases meet all of the criteria for protection under a statutory exception or regulatory safe harbor. Additionally, 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 federal false claims laws, including the False Claims Act, which prohibit, among other things, any person or entity from knowingly presenting, or causing to be presented, a false claim for payment to, or approval by, the federal government or knowingly making, using, or causing to be made or used a false record or statement material to a false or fraudulent claim to the federal government. As a result of a modification made by the Fraud Enforcement and Recovery Act of 2009, a claim under the False Claims Act includes “any request or demand” for money or property presented to the U.S. government. The federal civil False Claims Act can be enforced through private “qui tam” actions brought by individual whistleblowers in the name of the government. In addition, manufacturers can be held liable under the civil 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. Pharmaceutical and other healthcare companies have been prosecuted under these laws for, among other things, allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product and for causing false claims to be submitted because of the companies’ marketing of the product for unapproved, and thus non-covered, uses. In addition, a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal False Claims Act.

The federal Health Insurance Portability and Accountability Act of 1996 (HIPAA) also created new federal criminal statutes that prohibit, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud or to obtain, by means of false or fraudulent pretenses, representations or promises, any money or property owned by, or under the control or custody of, any healthcare benefit program, including private third-party payors and knowingly and willfully falsifying, concealing or covering up by trick, scheme or device, a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. Similar to the 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. Also, many states have similar fraud and abuse statutes or regulations that apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor.

Additionally, the federal Physician Payments Sunshine Act, and its implementing regulations, require that certain manufacturers of drugs, devices, biological and medical supplies for which payment is available under Medicare, Medicaid or the Children’s Health Insurance Program (with certain exceptions) annually report information related to certain payments or other transfers of value made or distributed to physicians (currently defined to include doctors, dentists, optometrists, podiatrists and chiropractors), other healthcare professionals (such as physician assistants and nurse practitioners), and teaching hospitals and certain ownership and investment interests held by physicians and their immediate family members.

In order to distribute products commercially, we must comply with state laws that require the registration of manufacturers and wholesale distributors of pharmaceutical products in a state, including, in certain states, manufacturers and distributors who ship products into the state even if such manufacturers or distributors have no place of business within the state. Some states also impose requirements on manufacturers and distributors to establish the pedigree of product in the chain of distribution, including some states that require manufacturers and others to adopt new technology capable of tracking and tracing product as it moves through the distribution chain. Several states have enacted legislation requiring pharmaceutical companies to establish marketing compliance programs, file periodic reports with the state, make periodic public disclosures on sales, marketing, pricing, track and report gifts, compensation and other remuneration made to physicians and other healthcare providers, clinical trials and other activities, and/or register their sales representatives, as well as to prohibit pharmacies and other healthcare entities from providing certain physician prescribing data to pharmaceutical companies for use in sales and marketing, and to prohibit certain other sales and marketing practices. All of our activities are also potentially subject to federal and state consumer protection and unfair competition laws.

If our operations are found to be in violation of any of the federal and state healthcare laws described above or any other governmental regulations that apply to us, we may be subject to significant penalties, including without limitation, civil, criminal and/or administrative penalties, damages, fines, disgorgement, imprisonment, exclusion from participation in government programs, such as Medicare and Medicaid, injunctions, private “qui tam” actions brought by individual whistleblowers in the name of the government, or refusal to allow us to enter into government contracts, contractual damages, reputational harm, administrative burdens, diminished profits and future earnings, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

Data Privacy and Security

We may also be subject to data privacy and security regulations by both the federal government and the states in which we conduct our business. For example, HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act (HITECH) and regulations implemented thereunder, imposes obligations on “covered entities,” including certain health care providers, health plans, and health care clearinghouses, and their respective “business associates” and covered subcontractors that create, receive, maintain or transmit individually identifiable health information for or on behalf of a covered entity, as well as their covered subcontractors with respect to the privacy, security and transmission of individually identifiable health information. Entities that are found to be in violation of HIPAA, whether as the result of a breach of unsecured PHI, a complaint about privacy practices, or an audit by the U.S. Department of Health and Human Services (HHS), may be subject to significant civil, criminal, and administrative fines and penalties and/or additional reporting and oversight obligations if required to enter into a resolution agreement and corrective action plan with HHS to settle allegations of HIPAA non-compliance.

In addition, state laws govern the privacy and security of health information in specified circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts. For example, California recently enacted the California Consumer Privacy Act (CCPA), which went into effect on January 1, 2020. The CCPA creates individual privacy rights for California consumers (as defined in the law) and places increased privacy and security obligations on entities handling certain personal data of consumers or households. The CCPA requires covered businesses to provide new disclosure to consumers about such business’ data collection, use and sharing practices, provide such consumers new ways to opt-out of certain sales or transfers of personal information, and provide consumers with additional causes of action. The CCPA provides for civil penalties for violations, as well as a private right of action for data breaches that is expected to increase data breach litigation. Additionally, a new privacy law, the California Privacy Rights Act (CPRA), was approved by California voters on November 3, 2020 and went into effect on January 1, 2023. The CPRA modifies significantly the CCPA, potentially resulting in further uncertainty and requiring us to incur additional costs and expenses in an effort to comply. Both the CCPA and CPRA could impact our business activities depending on how they are interpreted and exemplifies the vulnerability of our business to not only cyber threats but also the evolving regulatory environment related to personal data and protected health information.

We also are or will become subject to applicable privacy laws in the jurisdictions in which we are established or in which we sell or market our products or run clinical trials. For example, if we conduct EU-based clinical trials, we will be subject to Regulation (EU) 2016/679, the General Data Protection Regulation (GDPR) in relation to our collection, control, processing and other use of personal data of EU-based data subjects (i.e. data relating to an identifiable living individual). We process personal data in relation to participants in our clinical trials in the European Economic Area (EEA), including the health and medical data of these participants. The GDPR is directly applicable in each EU and EEA Member State, however, it provides that EU and EEA Member States may introduce further conditions, including limitations which could limit our ability to collect, control, process and otherwise use and share personal data (including health and medical data), or could cause our compliance costs to increase, ultimately having an adverse impact on our business. The GDPR imposes onerous accountability obligations requiring data controllers and processors to maintain a record of their data processing activities and implement policies as part of its mandated privacy governance framework. It also requires data controllers to be transparent and disclose to data subjects (in a concise, intelligible and easily accessible form) how their personal data is to be used, imposes limitations on retention of personal data; defines pseudonymized (i.e., key-coded) data; introduces mandatory data breach notification requirements; and sets higher standards for data controllers to demonstrate that they have obtained valid consent for certain data processing activities. We are also subject to EU rules with respect to cross-border transfers of personal data out of the EU and EEA. Although there are currently various mechanisms that may be used to transfer personal data from the EEA to the United States in compliance with law, such as the EU's standard contractual clauses, these mechanisms are subject to legal challenges, and there is no assurance that we can satisfy or rely on these measures to lawfully transfer personal data to the United States. We are subject to the supervision of local data protection authorities in those EU jurisdictions where we are established or otherwise subject to the GDPR, and we maintain an office in Switzerland, which has its own set of stringent privacy and data protection laws and regulations. Fines for certain breaches of the GDPR are significant: up to the greater of €20 million or 4% of total global annual turnover. In addition to the foregoing, a breach of the GDPR or other applicable privacy and data protection laws and regulations could result in regulatory investigations, reputational damage, orders to cease/change our use of data, enforcement notices, or potential civil claims including class action type litigation.

Further, the United Kingdom (UK)'s withdrawal from the EU and the EEA has created uncertainty with regard to data protection regulation in the UK. Specifically, while the Data Protection Act of 2018, which implements and complements the GDPR in the UK, it is uncertain how UK data protection laws and regulations will develop in the medium to longer term, and how data transfers to and from the UK will be regulated in the long term. On June 28, 2021, the European Commission adopted an adequacy decision permitting flows of personal data between the EU and the UK to continue without additional requirements. The UK Government also adopted a reciprocal adequacy decision in respect of EEA member states permitting flows of personal data from the UK to the EEA. However, the European Commission's UK adequacy decision will automatically expire in June 2025 unless the European Commission re-assesses and renews/extends that decision and remains under review by the European Commission during this period.

Pharmaceutical Coverage, Pricing and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any product candidates for which we or our collaborators obtain regulatory approval. In the United States and markets in other countries, sales of any products for which we receive regulatory approval for commercial sale will depend, in part, on the extent to which third-party payors provide coverage, and establish adequate reimbursement levels for such drug products.

In the United States, third-party payors include federal and state healthcare programs, government authorities, private managed care providers, private health insurers and other organizations. Third-party payors are increasingly challenging the price, examining the medical necessity and reviewing the cost-effectiveness of medical drug products and medical services, in addition to questioning their safety and efficacy. Such payors may limit coverage to specific drug products on an approved list, also known as a formulary, which might not include all of the FDA-approved drugs for a particular indication. We or our collaborators may need to conduct expensive pharmaco-economic studies in order to demonstrate the medical necessity and cost-effectiveness of our products, in addition to the costs required to obtain the FDA approvals. Nonetheless, our product candidates may not be considered medically necessary or cost-effective. Moreover, the process for determining whether a third-party payor will provide coverage for a drug product may be separate from the process for setting the price of a drug product or for establishing the reimbursement rate that such a payor will pay for the drug product. A payor's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Further, no uniform policy for coverage and reimbursement exists in the United States, and coverage and reimbursement can differ significantly from payor to payor. As a result, one payor's determination to provide coverage for a drug product does not assure that other payors will also provide coverage for the drug product. For gene therapy and other 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. Adequate third-party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development.

If we elect to participate in certain governmental programs, we may be required to participate in discount and rebate programs, which may result in prices for our future products that will likely be lower than the prices we might otherwise obtain. For example, drug manufacturers participating under the Medicaid Drug Rebate Program must pay rebates on prescription drugs to state Medicaid programs.

Different pricing and reimbursement schemes exist in other countries. In the EU, governments influence the price of pharmaceutical products through their pricing and reimbursement rules and control of national health care systems that fund a large part of the cost of those products to consumers. Some jurisdictions operate positive and negative list systems under which products may only be marketed once a reimbursement price has been agreed. To obtain reimbursement or pricing approval, some of these countries may require the completion of clinical trials that compare the cost-effectiveness of a particular product candidate to currently available therapies. Other member states allow companies to fix their own prices for medicines, but monitor and control company profits. The downward pressure on health care costs in general, particularly prescription drugs, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, in some countries, cross-border imports from low-priced markets exert a commercial pressure on pricing within a country.

The marketability of any product candidates for which we or our collaborators receive regulatory approval for commercial sale may suffer if the government and third-party payors fail to provide adequate coverage and reimbursement. In addition, emphasis on managed care in the United States has increased and we expect will continue to increase the pressure on pharmaceutical pricing. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which we or our collaborators receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Healthcare Reform

A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and other third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medical products and services, implementing reductions in Medicare and other healthcare funding and applying new payment methodologies. For example, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act (collectively ACA), was enacted, which affected existing government healthcare programs and resulted in the development of new programs.

Among the ACA's provisions of importance to the pharmaceutical industry, in addition to those otherwise described above, are the following:

- an annual, nondeductible fee on any entity that manufactures or imports certain specified branded prescription drugs and biologic agents apportioned among these entities according to their market share in some government healthcare programs;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% and 13% of the average manufacturer price for most branded and generic drugs, respectively, and a cap on the total rebate amount for innovator drugs at 100% of the Average Manufacturer Price (AMP);
- 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 manufacturers' outpatient drugs to be covered under Medicare Part D;
- extension of manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals, including individuals with income at or below 133% of the federal poverty level, thereby potentially increasing manufacturers' Medicaid rebate liability;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program; and
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

There have been executive judicial and Congressional challenges to certain aspects of the ACA. For example, on June 17, 2021 the U.S. Supreme Court dismissed a challenge on procedural grounds that argued the ACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress. Further, prior to the U.S. Supreme Court ruling, on January 28, 2021, President Biden issued an executive order that initiated a special enrollment period from February 15, 2021 through May 15, 2021 for purposes of obtaining health insurance coverage through the ACA marketplace. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. On August 16, 2022, President Biden signed the Inflation Reduction Act of 2022, or IRA, into law, which, among other things, extends enhanced subsidies for individuals purchasing health insurance coverage in ACA marketplaces through plan year 2025. The IRA also eliminates the "donut hole" under the Medicare Part D program beginning in 2025 by significantly lowering the beneficiary maximum out-of-pocket cost and creating a new manufacturer discount program. It is unclear how any additional challenges or additional healthcare reform measures of the Biden administration will impact the ACA or our business.

Other legislative changes have also been proposed and adopted in the United States since the Healthcare Reform Act was enacted. On August 2, 2011, the Budget Control Act of 2011, among other things, included aggregate reductions to Medicare payments to providers of 2% per fiscal year, which went into effect on April 1, 2013 and, due to subsequent legislative amendments to the statute, will remain in effect through 2031, with the exception of a temporary suspension from May 1, 2020 through March 31, 2022, unless additional Congressional action is taken. Under current legislation, the actual reduction in Medicare payments will vary from 1% in 2022 to up to 4% in the final fiscal year of this sequester. In January 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. There has been heightened governmental scrutiny recently over the manner in which pharmaceutical companies set prices for their marketed products, which has resulted in several Congressional inquiries and proposed federal legislation, additional federal regulations, as well as state efforts, designed to, among other things, bring more transparency to product pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products.

Recently, there has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices. Specifically, there have been several recent congressional inquiries and legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs and reform government program reimbursement methodologies for drugs. At the federal level, in July 2021, the Biden administration released an executive order, “Promoting Competition in the American Economy,” with multiple provisions aimed at prescription drugs. In response to Biden’s executive order, on September 9, 2021, HHS released a Comprehensive Plan for Addressing High Drug Prices that outlines principles for drug pricing reform and sets out a variety of potential legislative policies that Congress could pursue to advance these principles. In addition, the IRA, among other things, (i) directs HHS to negotiate the price of certain high-expenditure, single-source drugs and biologics covered under Medicare, and subject drug manufacturers to civil monetary penalties and a potential excise tax by offering a price that is not equal to or less than the negotiated “maximum fair price” for such drugs and biologics under the law, and (ii) imposes rebates with respect to certain drugs and biologics covered under Medicare Part B or Medicare Part D to penalize price increases that outpace inflation. The IRA permits HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years. These provisions will take effect progressively starting in fiscal year 2023, although they may be subject to legal challenges. It is currently unclear how the IRA will be implemented but is likely to have a significant impact on the pharmaceutical industry. Further, the Biden administration released an additional executive order on October 14, 2022, directing HHS to submit a report on how the Center for Medicare and Medicaid Innovation can be further leveraged to test new models for lowering drug costs for Medicare and Medicaid beneficiaries. It is unclear whether this executive order or similar policy initiatives will be implemented in the future. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control costs pharmaceutical and biological products. Moreover, 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.

We anticipate that these new laws will result in additional downward pressure on coverage and the price that we receive for any approved product, and could seriously harm our business. Any reduction in reimbursement from Medicare and other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our products. In addition, it is possible that there will be further legislation or regulation that could harm our business, financial condition, and results of operations. Additionally, health reform initiatives may arise in the future.

The U.S. Foreign Corrupt Practices Act

The U.S. Foreign Corrupt Practices Act of 1977 (FCPA) prohibits any U.S. individual or business from paying, offering, or authorizing payment or offering of anything of value, directly or indirectly, to any foreign official, political party 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 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.

Europe / Rest of World Government Regulation

In addition to regulations in the United States, we will be subject to a variety of regulations in other jurisdictions governing, among other things, clinical trials and any commercial sales and distribution of our products. Whether or not we or our potential collaborators obtain FDA approval for a product, we must obtain the requisite approvals from regulatory authorities in foreign countries prior to the commencement of clinical trials or marketing of the product in those countries. Certain countries outside of the United States have a similar process that requires the submission of an application for a clinical trial authorization (CTA) much like the IND prior to the commencement of human clinical trials. In the EU, for example, a CTA must be submitted to each country's national health authority and an application made to an independent ethics committee, much like the FDA and IRB, respectively. Once the CTA is approved in accordance with a country's requirements and a favorable ethics committee opinion has been issued, clinical trial development may proceed.

The requirements and process governing the conduct of clinical trials are to a significant extent harmonized at the EU level, but could vary from country to country. In all cases, the clinical trials must be conducted in accordance with GCP and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki. The way clinical trials are conducted in the EU will undergo a major change when the Clinical Trial Regulation (Regulation (EU) No 536/2014) comes into application, expected in 2022.

To obtain regulatory approval of an investigational drug or biological product under EU regulatory systems, we must submit a marketing authorization application either under the so-called centralized or national authorization procedures. The application used to file an NDA in the United States is similar to that required in the European Union, but the exact requirements for authorization may vary.

Centralized Procedure. The centralized procedure provides for the grant of a single marketing authorization by the European Commission following a favorable opinion by the European Medicines Agency (EMA) that is valid in all EU member states, as well as Iceland, Liechtenstein and Norway. The centralized procedure is compulsory for medicines produced by specified biotechnological processes, products designated as orphan medicinal products, and products with a new active substance indicated for the treatment of specified diseases, such as HIV/AIDS, cancer, diabetes, neurodegenerative disorders or autoimmune diseases, other immune dysfunctions and viral diseases. The centralized procedure is optional for other products that represent a significant therapeutic, scientific or technical innovation, or whose authorization would be in the interest of public health or which contain a new active substance for indications other than those specified to be compulsory.

National Authorization Procedures. There are also two other possible routes to authorize medicinal products in several EU countries, which are available for investigational medicinal products that fall outside the scope of the centralized procedure:

- ***Decentralized Procedure.*** Using the decentralized procedure, an applicant may apply for simultaneous authorizations in more than one EU Member State of medicinal products that have not yet been authorized in any EU Member State and that do not fall within the mandatory scope of the centralized procedure.
- ***Mutual Recognition Procedure.*** In the mutual recognition procedure, a medicine is first authorized in one EU Member State, in accordance with the national procedures of that country. Following this, further marketing authorizations can be sought from other EU countries in a procedure whereby the countries concerned agree to recognize the validity of the original, national marketing authorization.

The European Union also provides opportunities for market exclusivity. For example, upon receiving marketing authorization, new chemical entities generally receive eight years of data exclusivity and an additional two years of market exclusivity. If granted, data exclusivity prevents regulatory authorities in the European Union from referencing the innovator's data to assess a generic or biosimilar application. During the additional two-year period of market exclusivity, a generic or biosimilar marketing authorization can be submitted, and the innovator's data may be referenced, but no generic or biosimilar product can be marketed until the expiration of the market exclusivity. However, there is no guarantee that a product will be considered by the European Union's regulatory authorities to be a new chemical entity, and products may not qualify for data exclusivity.

The EMA grants orphan drug designation to promote the development of products for the treatment, prevention or diagnosis of life-threatening or chronically debilitating conditions affecting not more than five in 10,000 people in the EU. In addition, orphan drug designation can be granted if the drug is intended for a life threatening or chronically debilitating condition in the EU and without incentives it is unlikely that sales of the drug in the EU would be sufficient to justify the investment required to develop the drug. Orphan drug designation is only available if there is no other satisfactory method approved in the EU of diagnosing, preventing or treating the condition, or if such a method exists, the proposed orphan drug will be of significant benefit to patients. Orphan drug designation provides opportunities for free or reduced-fee protocol assistance, fee reductions for marketing authorization applications and other post-authorization activities and ten years of market exclusivity following drug approval, which can be extended to 12 years if trials are conducted in accordance with an agreed-upon pediatric investigational plan. The exclusivity period may be reduced to six years if the designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

In the European Union, early access mechanisms for innovative medicines (such as compassionate use programs and named patient supplies), pricing and reimbursement, and promotion and advertising, amongst other things, are subject to national regulations and oversight by national competent authorities and therefore significantly vary from country to country.

Sanctions for non-compliance with the aforementioned requirements, which may include administrative and criminal penalties, are generally determined and enforced at national level. However, under the EU financial penalties regime, the EMA can investigate and report on alleged breaches of the EU pharmaceutical rules by holders of a marketing authorization for centrally authorized medicinal products and the European Commission could adopt decisions imposing significant financial penalties on infringing marketing authorization holders.

The United Kingdom left the European Union on January 31, 2020. Following the transition period which ended on December 31, 2020, Brexit could materially impact the regulatory regime with respect to the development, manufacture, importation, approval and commercialization of our product candidates in the United Kingdom in the coming years.

For other countries outside of the EU, 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. In all cases, again, the clinical trials are conducted in accordance with GCP and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

If we or our potential collaborators 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.

Corporate Information

We were incorporated under the laws of the State of Delaware on December 18, 2017. Our principal executive offices are located at 6005 Hidden Valley Road, Suite 110, Carlsbad, California 92011, and our telephone number is (858) 293-4900. Our corporate website address is www.designtx.com. We make available, free of charge on our website our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, and any amendments to those reports, as soon as reasonably practicable after filing such reports with the SEC. Information contained on, or accessible through, our website shall not be deemed incorporated into and is not a part of this Annual Report on Form 10-K. We have included our website in this Annual Report on Form 10-K solely as an inactive textual reference.

Employees and Human Capital Resources

As of December 31, 2022, we had 58 employees, all of whom were full-time, and 23 of whom have a Ph.D. or M.D. 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. In addition, we also utilize specialized contract research organizations for additional research and development personnel. Together with our employees, our team comprised approximately 132 full-time equivalents as of December 31, 2022.

Our human capital resources objectives include, as applicable, identifying, recruiting, retaining, incentivizing and integrating our existing and additional employees. The principal purposes of our equity incentive plans are to attract, retain and motivate selected employees, consultants and directors through the granting of stock-based compensation awards.

Item 1A. Risk Factors.

We operate in a dynamic and rapidly changing environment that involves numerous risks and uncertainties. Certain factors may have a material adverse effect on our business, financial condition and results of operations, and you should carefully consider them. Accordingly, in evaluating our business, we encourage you to consider the following discussion of risks described below, together with the other information contained in this Annual Report on Form 10-K and in our other public filings with the Securities and Exchange Commission (SEC). If any of the following risks actually occur, our business, financial condition, results of operations, and future growth prospects would likely be materially and adversely affected. In these circumstances, the market price of our common stock would likely decline. Other events that we do not currently anticipate or that we currently deem immaterial may also affect our results of operations and financial condition.

Risks Related to Our Limited Operating History, Financial Position and Capital Requirements

We have a limited operating history, have incurred net losses since our inception, and anticipate that we will continue to incur significant losses for the foreseeable future. We may never generate any revenue or become profitable or, if we achieve profitability, may not be able to sustain it.

We are a clinical-stage biopharmaceutical company with a limited operating history that may make it difficult to evaluate the success of our business to date and to assess our future viability. Our operations to date have been limited to business planning, organizing and staffing our company, raising capital, developing and optimizing our technology platform, identifying potential product candidates, undertaking research and preclinical studies for our lead program and our other development programs, early clinical development for our lead program, establishing and enhancing our intellectual property portfolio, and providing general and administrative support for these operations. In March 2022, we completed dosing in the first cohort for the single-ascending dose (SAD) Phase 1 clinical trial of DT-216, our lead FA GeneTAC™ product candidate. We announced initial data from our SAD Phase 1 clinical trial in December 2022. We have initiated patient dosing in the ongoing multiple-ascending dose (MAD) Phase 1 clinical trial of DT-216. All other product candidates are in preclinical development, and none have been approved for commercial sale. We have never generated any revenue from product sales and have incurred net losses each year since we commenced operations, including a net loss of \$63.3 million and \$35.5 million for the years ended December 31, 2022 and 2021, respectively. We expect that it will be several years, if ever, before we have a product candidate ready for regulatory approval and commercialization. We expect to incur increasing levels of operating losses over the next several years and for the foreseeable future as we advance our product candidates through clinical development. Our prior losses, combined with expected future losses, have had and will continue to have an adverse effect on our stockholders' equity and working capital.

To become and remain profitable, we must develop and eventually commercialize a product or products with significant market potential. This will require us to be successful in a range of challenging activities, including completing preclinical studies and clinical trials of our product candidates, obtaining marketing approval for these product candidates, manufacturing, marketing and selling those products for which we may obtain marketing approval and satisfying any post-marketing requirements. We may never succeed in these activities and, even if we succeed in commercializing one or more of our product candidates, we may never generate revenue that is significant or large enough to achieve profitability. In addition, as a young business, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown challenges. If we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis and we will continue to incur substantial research and development and other expenditures to develop and market additional product candidates. Our failure to become and remain profitable would decrease the value of the company and could impair our ability to raise capital, maintain our research and development efforts, expand our business or continue our operations. A decline in the value of our company could also cause you to lose all or part of your investment.

If we are unable to raise additional capital when needed, we may be forced to delay, reduce or eliminate our product development programs or other operations.

Since our inception, we have used substantial amounts of cash to fund our operations and expect our expenses to increase substantially during the next few years. The development of biopharmaceutical product candidates is capital intensive. As our product candidates enter and advance through preclinical studies and clinical trials, we will need substantial additional funds to expand our clinical, regulatory, quality and manufacturing capabilities. In addition, if we obtain marketing approval for any of our product candidates, we expect to incur significant commercialization expenses related to marketing, sales, manufacturing and distribution.

As of December 31, 2022, we had \$330.4 million in cash, cash equivalents and investment securities. Based upon our current operating plan, we estimate that our existing cash, cash equivalents and investment securities will be sufficient to fund our operating expenses and capital expenditure requirements for more than the next 12 months. However, we believe that our existing cash, cash equivalents and investment securities will not be sufficient to fund any of our product candidates through regulatory approval, and we will need to raise substantial additional capital to complete the development and commercialization of our product candidates.

We have based these estimates on assumptions that may prove to be incorrect or require adjustment as a result of business decisions, and we could utilize our available capital resources sooner than we currently expect. Our future capital requirements will depend on many factors, including:

- the scope, rate of progress and costs of our drug discovery, preclinical development activities, laboratory testing and clinical trials for any current or future product candidates;
- the number and scope of clinical programs we decide to pursue;
- the scope and costs of manufacturing our product candidates and any future commercial manufacturing activities;
- the emergence of competing therapies and other adverse market developments;
- the cost, timing and outcome of seeking FDA, EMA and any other regulatory approvals for any product candidates;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;
- the terms and timing of establishing and maintaining strategic collaborations, licenses and other similar arrangements and the financial terms of such agreements;
- our efforts to enhance operational systems and our ability to attract, hire and retain qualified personnel, including personnel to support the development of our product candidates;
- the costs associated with being a public company;
- the timing of any milestone and royalty payments to WARF, or other future licensors;
- the extent to which we acquire or in-license other product candidates and technologies;
- our need and ability to retain key management and hire scientific, technical, medical and business personnel;
- our implementation of additional internal systems and infrastructure, including operational, financial and management information systems;
- or costs associated with expanding our facilities or building out additional laboratory space;

- the effects of the disruptions to and volatility in the credit and financial markets in the United States and worldwide from the ongoing military conflict initiated by Russia against Ukraine and actions taken by the U.S. and other governments in response, global supply chain and labor shortage challenges, inflation, high interest rates, COVID-19 or other health epidemic or pandemic, or as a result of macroeconomic factors; and
- the cost associated with commercialization activities for any of our product candidates, if approved.

Because we do not expect to generate revenue from product sales for many years, if at all, we will need to obtain substantial additional funding in connection with our continuing operations and expected increases in expenses. 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 or other similar arrangements. In addition, we may seek additional capital due to favorable market conditions or strategic considerations, even if we believe we have sufficient funds for our current or future operating plans. The impact of geopolitical events, health epidemics or pandemics and other macroeconomic factors on capital markets may affect the availability, amount and type of financing available to us in the future. If we are unable to raise capital when needed or on attractive terms, we would be forced to delay, reduce or eliminate our research and development programs or future commercialization efforts.

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 revenue from product sales to support our cost structure, we expect to finance our operations through public or private equity offerings, debt financings or other capital sources, which may include strategic collaborations, licensing arrangements or other similar arrangements with third parties. To the extent that we raise additional capital through the sale of equity or convertible debt securities, current 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 existing stockholders. Equity and debt 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 strategic collaborations, or other similar 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 and/or may reduce the value of our common stock. 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 product candidates that we would otherwise prefer to develop and market ourselves. Our ability to raise additional funds may be adversely impacted by potential worsening global economic conditions and disruptions to and volatility in the credit and financial markets in the United States and worldwide resulting from the ongoing military conflict initiated by Russia against Ukraine and actions taken by the U.S. and other governments in response, global supply chain and labor shortage challenges, inflation, high interest rates, COVID-19 or other health epidemic or pandemic, or otherwise. Because of the numerous risks and uncertainties associated with product development, we cannot predict the timing or amount of increased expenses and cannot assure you that we will ever be profitable or generate positive cash flow from operating activities.

Risks Related to the Discovery, Development and Regulatory Approval of Our Product Candidates

We are early in our development efforts and we have only one product candidate in clinical development, with all other research programs still in the preclinical or discovery stage. We have a limited history of conducting clinical trials to test our product candidates in humans.

We are early in our development efforts and most of our operations to date have been limited to developing our platform technologies and conducting drug discovery and preclinical studies. Our lead FA GeneTAC™ product candidate, DT-216, entered into a Phase 1 clinical trial in March 2022, the first clinical trial for one of our product candidates and we have also initiated patient dosing in the ongoing MAD Phase 1 clinical trial of DT-216. As a result, we have limited infrastructure, experience conducting clinical trials as a company and regulatory interactions, and cannot be certain that our ongoing and planned clinical trials will be completed on time, if at all, that our planned development programs would be acceptable to the FDA or other comparable foreign regulatory authorities, or that, if approval is obtained, such product candidates can be successfully commercialized.

Because of the early stage of development of our products candidates, our ability to eventually generate significant revenues from product sales will depend on a number of factors, including:

- completion of preclinical studies and clinical trials with favorable results;
- acceptance of INDs by the FDA or similar regulatory filing by comparable foreign regulatory authorities for the conduct of clinical trials of our product candidates and our proposed design of future clinical trials;
- receipt of marketing approvals from applicable regulatory authorities, including new drug applications (NDAs), from the FDA and maintaining such approvals;
- market acceptance of any of our approved product candidates;
- making arrangements with our third-party manufacturers for, or establishing, commercial manufacturing capabilities;
- maintaining an acceptable safety profile of our products following approval; and
- maintaining and growing an organization of scientists and business personnel who can develop our products and technology.

The success of our business, including our ability to finance our company and generate any revenue in the future, will primarily depend on the successful development, regulatory approval and commercialization of our FA, FECD and DM1 GeneTAC™ candidates, as well as our other product candidates, which may never occur. In the future, we may also become dependent on other product candidates that we may develop or acquire; however, given our early stage of development, it may be several years, if at all, before we have demonstrated the safety and efficacy of a treatment sufficient to warrant approval for commercialization. If we are unable to develop, or obtain regulatory approval for, or, if approved, successfully commercialize our product candidates, we may not be able to generate sufficient revenue to continue our business.

Preclinical and clinical development involves a lengthy and expensive process with uncertain timelines and outcomes, and results of preclinical studies and clinical trials may not be predictive of future trial results. If development of our programs is unsuccessful or delayed, we may be unable to obtain required regulatory approvals and be unable to commercialize our product candidates on a timely basis, if at all.

Clinical drug development is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure or delay can occur at any time during the drug development process, including due to factors outside of our control. Success in nonclinical testing and early clinical trials does not ensure that later clinical trials will be successful. A number of companies in the pharmaceutical industry, including biotechnology companies, have suffered significant setbacks in clinical trials, even after promising results in earlier nonclinical studies or clinical trials. These setbacks have been caused by, among other things, nonclinical findings made while clinical trials were underway and safety or efficacy observations made in clinical trials, including previously unreported adverse events. The results of preclinical, nonclinical and early clinical trials of our product candidates may not be predictive of the results of later-stage clinical trials. In particular, while we have conducted preclinical studies of DT-216 and have released initial clinical data from our SAD Phase 1 clinical trial on December 7, 2022, we are still evaluating how DT-216 will perform throughout the MAD study portion of our Phase 1 clinical program or in future clinical trials or whether adverse events will arise over time. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy traits despite having progressed through preclinical and initial clinical trials. Notwithstanding any potential promising results in earlier studies, we cannot be certain that we will not face similar setbacks. Even if our clinical trials are completed, the results may not be sufficient to obtain regulatory approval for our product candidates.

We may experience delays in initiating our clinical trials for our product candidates and we cannot be certain that the trials or any other future clinical trials for our product candidates will begin on time, need to be redesigned, enroll an adequate number of patients on time or be completed on schedule, if at all. Clinical trials can be delayed or terminated for a variety of reasons, including delay or failure related to:

- the FDA or comparable foreign regulatory authorities disagreeing as to the design or implementation of our planned clinical trials, or the sufficiency of preclinical data to initiate clinical trials;
- the size of the study population for further analysis of the study's primary endpoints;
- obtaining regulatory approval to commence a trial;
- reaching agreement on acceptable terms with prospective contract research organizations (CROs) and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- obtaining institutional review board (IRB), approval at each site;
- recruiting suitable patients to participate in a trial;
- having patients complete a trial or return for post-treatment follow-up;
- clinical sites deviating from trial protocol or dropping out of a trial;
- addressing patient safety concerns that arise during the course of a trial;
- addressing any conflicts with new or existing laws or regulations;
- adding a sufficient number of clinical trial sites; or
- manufacturing sufficient quantities of product candidate for use in clinical trials.

We could also encounter delays if a clinical trial is suspended or terminated by us, by the IRBs of the institutions in which such trials are being conducted, by a Data Safety Monitoring Board (DSMB) for such trial or by the FDA or other regulatory authorities (including foreign regulatory authorities comparable to the FDA). 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 drug, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial.

Further, conducting clinical trials in foreign countries, as we plan 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.

Moreover, principal investigators for our ongoing or planned 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.

If we experience delays in the completion, or termination, of any clinical trial of our product candidates, the commercial prospects of our product candidates may be harmed, and our ability to generate product revenue from any of these product candidates will be delayed or not realized at all. In addition, any delays in completing our ongoing or planned clinical trials will increase our costs, slow down our product candidate development and approval process and jeopardize our ability to commence product sales and generate revenue. Any of these occurrences may significantly harm our business, financial condition and prospects. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates.

Our product candidates are based on novel technologies, which make it difficult to predict the timing, results and cost of product candidate development and likelihood of obtaining regulatory approval.

We have concentrated our research and development efforts on product candidates using our platform technologies, and our future success depends on the successful development of this approach. We have not yet succeeded and may not succeed in demonstrating efficacy and safety for any product candidates based on our platform technologies in clinical trials or in obtaining marketing approval thereafter, and use of our platform technologies may not ever result in marketable products. We may also experience delays in developing a sustainable, reproducible and scalable manufacturing process or transferring that process to commercial partners or establishing our own commercial manufacturing capabilities, which may prevent us from completing our ongoing or planned clinical trials or commercializing any products on a timely or profitable basis, if at all.

The clinical trial requirements of the FDA, EMA and other comparable foreign regulatory agencies and the criteria these regulators use to determine the safety and efficacy of a product candidate vary substantially according to the type, complexity, novelty and intended use and market of the potential products. The regulatory approval process for novel product candidates such as ours can be more expensive and take longer than for other, better known or extensively studied pharmaceutical or other product candidates.

The biotechnology and biopharmaceutical industries are also rapidly developing, and our competitors may introduce new technologies improving the treatments in the field of expansion repeat driven diseases and small molecules that render our technologies obsolete or less attractive. New technology could emerge at any point in the development cycle of our product candidates.

If we encounter difficulties or delays enrolling patients in our ongoing or planned clinical trials, our clinical development activities could be delayed or otherwise adversely affected.

We may not be able to continue our ongoing clinical trial or initiate or continue clinical trials planned in the future for our product candidates if we are unable to identify and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA. Patient enrollment, a significant factor in the timing of clinical trials, is affected by many factors including the size and nature of the patient population, the proximity of patients to clinical sites, the eligibility criteria for the clinical trial, the design of the clinical trial, competing clinical trials and clinicians' and patients' perceptions as to the potential advantages of the product candidate being studied in relation to other available therapies, including any new drugs that may be approved for the indications we are investigating.

The timely completion of clinical trials in accordance with their protocols depends, among other things, on our ability to enroll a sufficient number of patients who remain in the study until its conclusion. We may experience difficulties in patient enrollment or retention in our clinical trials for a variety of reasons. The enrollment of patients depends on many factors, including:

- the patient eligibility criteria defined in the protocol;
- the size of the patient population required for analysis of the trial's primary endpoints;
- the proximity of patients to study sites;
- the design of the trial;
- our ability to recruit clinical trial investigators with the appropriate competencies and experience;
- clinicians' and patients' perceptions as to the potential advantages of the product candidate being studied in relation to other available therapies, including any new drugs that may be approved for the indications we are investigating;
- our ability to obtain and maintain patient consents; and
- the risk that patients enrolled in clinical trials will drop out of the trials before completion.

In addition, our ongoing and planned clinical trials may compete with other clinical trials for product candidates that are in the same therapeutic areas as our product candidates, and this competition will reduce the number and types of patients available to us, because some patients who might have opted to enroll in our trials may instead opt to enroll in a trial being conducted by one of our competitors. We may also experience enrollment challenges if patients that would otherwise enroll in our trial choose not to do so, or are not eligible to do so, as a result of treatment with another drug. For example, Reata Pharmaceuticals announced on February 28, 2023 that the FDA approved omaveloxolone for the treatment of FA in adults and adolescents aged 16 years and older. The approval of omaveloxolone may impact future enrollment of our planned clinical trials. FA patients receiving omaveloxolone may be ineligible to enroll in a clinical trial for DT-216 or may choose not to do so due to the availability of an approved product. Furthermore, some patients enrolled in our clinical trials may be receiving omaveloxolone and we cannot predict the impact of potential drug interactions on trial results. Delays in patient enrollment may result in increased costs or may affect the timing or outcome of our ongoing or planned clinical trials, which could prevent completion of these trials and adversely affect our ability to advance the development of our product candidates.

We plan to conduct clinical trials for our product candidates outside the United States and the FDA may not accept data from such trials.

We plan to conduct additional clinical trials outside the United States. Although the FDA may accept data from clinical trials conducted outside the United States, acceptance of such study data by the FDA is subject to certain conditions. For example, the clinical trial must be conducted in accordance with Good Clinical Practices (GCP) requirements and the FDA must be able to validate the data from the clinical trial through an onsite inspection if it deems such inspection necessary.

Where data from foreign clinical trials are intended to serve as the sole 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 clinical trials 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. In addition, such clinical trials would be subject to the applicable local laws of the foreign jurisdictions where the clinical trials are conducted.

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 any such data, it would likely result in the need for additional clinical trials, which would be costly and time-consuming and delay aspects of our development plan. In addition, the conduct of clinical trials outside the United States could have a significant impact on us. Risks inherent in conducting international clinical trials include:

- foreign regulatory requirements that could burden or limit our ability to conduct our clinical trials;
- difficulties staffing and managing foreign operations;
- compliance with legal requirements applicable to privacy, data protection, information security and other matters;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign taxes, including value-added tax and withholding of payroll taxes;
- administrative burdens of conducting clinical trials under multiple foreign regulatory schema;
- foreign exchange fluctuations;
- manufacturing, customs, shipment and storage requirements;
- impact of geopolitical events or a public health crisis on our ability to produce our product candidates and conduct clinical trials in foreign countries;
- potential liability under the Foreign Corrupt Practices Act of 1977, as amended (FCPA), or comparable foreign regulations;
- cultural differences in medical practice and clinical research; and
- diminished protection of intellectual property in some countries.

Obtaining and maintaining regulatory approval of our product candidates in one jurisdiction does not mean that we will be successful in obtaining regulatory approval of our product candidates in other jurisdictions.

Obtaining and maintaining regulatory approval of our product candidates in one jurisdiction does not guarantee that we will be able to obtain or maintain regulatory approval in any other jurisdiction, while a failure or delay in obtaining regulatory approval in one jurisdiction may have a negative effect on the regulatory approval process in others. For example, even if the FDA grants marketing approval of a product candidate, comparable regulatory authorities in foreign jurisdictions must also approve the manufacturing, marketing and promotion of the product candidate in those countries. Approval procedures vary among jurisdictions and can involve requirements and administrative review periods different from, and greater than, those in the United States, including additional preclinical studies or clinical trials as clinical studies conducted in one jurisdiction may not be accepted by regulatory authorities in other jurisdictions. In many jurisdictions outside the United States, a product candidate must be approved for reimbursement before it can be approved for sale in that jurisdiction. In some cases, the price that we intend to charge for our products is also subject to approval.

Obtaining foreign regulatory approvals and compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our products in certain countries. If we fail to comply with the regulatory requirements in international markets and/or receive applicable marketing approvals, our target market will be reduced and our ability to realize the full market potential of our product candidates will be harmed.

Our product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, cause us to suspend or discontinue our ongoing or planned clinical trials, limit the commercial profile of an approved label, or result in significant negative consequences following marketing approval, if any.

Undesirable side effects caused by our product candidates could cause us or regulatory authorities to interrupt, delay or halt ongoing or planned clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or comparable foreign regulatory authorities. Results of our ongoing or planned clinical trials could reveal a high and unacceptable severity and prevalence of side effects or unexpected characteristics. For example, in December 2022, we reported initial data from the SAD clinical trial for our lead product candidate. Initial safety results from Cohorts 1-5 showed that DT-216 was generally well-tolerated after a single dose of DT-216, but three patients on DT-216 had injection site thrombophlebitis that were mild or moderate and resolved without treatment.

If unacceptable side effects, such as severe injection site reactions associated intravenous administration (including injection site thrombophlebitis), arise in the development of our product candidates, we, the FDA or comparable foreign regulatory authorities, the IRBs at the institutions in which our studies are conducted, or the DSMB (or applicable safety oversight committee) could recommend a protocol amendment, suspend or terminate our clinical trials or the FDA or deny approval of our product candidates for any or all targeted indications. Treatment-related side effects could also affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. In addition, these side effects may not be appropriately recognized or managed by the treating medical staff. We expect to have to train medical personnel using our product candidates to understand the side effect profiles for our clinical trials and upon any commercialization of any of our product candidates. Inadequate training in recognizing or managing the potential side effects of our product candidates could result in patient injury or death. Any of these occurrences may harm our business, financial condition and prospects significantly.

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

- we may be forced to suspend marketing of that product, or decide to remove the product from the marketplace;
- regulatory authorities may withdraw or change their approvals of that product;

- regulatory authorities may require additional warnings on the label or limit access of that product to selective specialized centers with additional safety reporting and with requirements that patients be geographically close to these centers for all or part of their treatment;
- we may be required to create a medication guide outlining the risks of the product for patients, or to conduct post-marketing studies;
- we may be required to change the way the product is administered;
- we could be subject to fines, injunctions, or the imposition of criminal or civil penalties, or be sued and held liable for harm caused to subjects or patients; and
- the product may become less competitive, and our reputation may suffer.

Any of the foregoing events could prevent us from achieving or maintaining market acceptance of the particular product candidate, if approved, and result in the loss of significant revenue to us, which would materially and adversely affect our results of operations and business.

Interim, topline and preliminary data from our preclinical studies or ongoing or planned 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 interim, preliminary or topline data from our preclinical studies or ongoing or planned 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. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the interim, 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. Interim, topline and preliminary 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, such data should be viewed with caution until the final data are available. From time to time, we may also disclose interim data from our clinical trials. Interim, topline, or preliminary data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Adverse differences between preliminary, interim or topline data and final data could significantly harm our business prospects.

Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular product candidate or product and our company in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is the material or otherwise appropriate information to include in our disclosure, and any information we determine not to disclose may ultimately be deemed significant with respect to future decisions, conclusions, views, activities or otherwise regarding a particular product, product candidate or our business. 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.

The regulatory approval process is lengthy, expensive and uncertain, and we may be unable to obtain regulatory approval for our product candidates under applicable regulatory requirements. The denial or delay of any such approval would delay commercialization of our product candidates and adversely impact our ability to generate revenue, our business and our results of operations.

The development, research, testing, manufacturing, labeling, approval, selling, import, export, marketing, promotion and distribution of drug products are subject to extensive and evolving regulation by federal, state and local governmental authorities in the United States, principally the FDA, and by foreign regulatory authorities, which regulations differ from country to country. Neither we nor any future collaborator is permitted to market any of our product candidates in the United States until we receive regulatory approval of an NDA from the FDA.

Obtaining regulatory approval of an NDA can be a lengthy, expensive and uncertain process. Prior to obtaining approval to commercialize a product candidate in the United States or abroad, we or our collaborators must demonstrate with substantial evidence from well-controlled clinical trials, and to the satisfaction of the FDA or other foreign regulatory agencies, that such product candidates are safe and effective for their intended uses. The number of nonclinical studies and clinical trials that will be required for FDA approval varies depending on the product candidate, the disease or condition that the product candidate is designed to address, and the regulations applicable to any particular product candidate.

Results from nonclinical studies and clinical trials can be interpreted in different ways. Even if we believe the nonclinical or clinical data for our product candidates are promising, such data may not be sufficient to support approval by the FDA and other regulatory authorities. Administering product candidates to humans may produce undesirable side effects, which could interrupt, delay or halt clinical trials and result in the FDA or other regulatory authorities denying approval of a product candidate for any or all indications. The FDA may also require us to conduct additional studies or trials for our product candidates either prior to or post-approval, such as additional drug-drug interaction studies or safety or efficacy studies or trials, or it may object to elements of our clinical development program such as the number of subjects in our clinical trials from the United States.

The FDA or any foreign regulatory bodies can delay, limit or deny approval of our product candidates or require us to conduct additional nonclinical or clinical testing or abandon a program for many reasons, including:

- the FDA or the applicable foreign regulatory agency's disagreement with the design or implementation of our planned clinical trials;
- negative or ambiguous results from our clinical trials or results that may not meet the level of statistical significance required by the FDA or comparable foreign regulatory agencies for approval;
- serious and unexpected drug-related side effects experienced by participants in our clinical trials or by individuals using drugs similar to our product candidates;
- our inability to demonstrate to the satisfaction of the FDA or the applicable foreign regulatory body that our product candidates are safe and effective for the proposed indication;
- the FDA's or the applicable foreign regulatory agency's disagreement with the interpretation of data from nonclinical studies or clinical trials; our inability to demonstrate the clinical and other benefits of our product candidates outweigh any safety or other perceived risks;
- the FDA's or the applicable foreign regulatory agency's requirement for additional nonclinical studies or clinical trials;
- the FDA's or the applicable foreign regulatory agency's disagreement regarding the formulation, labeling and/or the specifications of our product candidates;
- the FDA's or the applicable foreign regulatory agency's failure to approve the manufacturing processes or facilities of third-party manufacturers with which we contract; or

- the potential for approval policies or regulations of the FDA or the applicable foreign regulatory agencies to significantly change in a manner rendering our clinical data insufficient for approval.

Of the large number of drugs in development, only a small percentage successfully complete the FDA or other regulatory approval processes and are commercialized. The lengthy approval process as well as the unpredictability of ongoing and future clinical trial results may result in our failing to obtain regulatory approval to market our product candidates, which would significantly harm our business, financial condition, results of operations and prospects.

Even if we eventually complete our ongoing and planned clinical testing and receive approval of an NDA or foreign marketing application for our product candidates, the FDA or the applicable foreign regulatory agency may grant approval contingent on the performance of costly additional clinical trials, including Phase 4 clinical trials, and/or in the case of the FDA, the implementation of a Risk Evaluation and Mitigation Strategy (REMS), which may be required to ensure safe use of the drug after approval. The FDA or the applicable foreign regulatory agency may also approve a product candidate for a more limited indication or a narrower patient population than we originally requested, and the FDA or applicable foreign regulatory agency may not approve the labeling that we believe is necessary or desirable for the successful commercialization of a product candidate. Any delay in obtaining, or inability to obtain, applicable regulatory approval would delay or prevent commercialization of that product candidate and would materially adversely impact our business and prospects.

A health epidemic or pandemic could adversely impact our business and affect our operations, as well as the business or operations of our manufacturers or other third parties with whom we conduct business.

Our business could be adversely affected by the effects of health epidemics or pandemics in regions where we have business operations, and could cause significant disruption in the operations of third parties upon whom we rely including our suppliers, CROs and other contract service providers. Measures imposed by governments in affected regions may impact commercial activities and businesses in an effort to reduce the spread of the disease. We may experience disruptions that could severely impact our business and clinical trials, including:

- delays or difficulties in enrolling and retaining patients in our clinical trials, particularly subjects who are at a higher risk of severe illness or death;
- delays or difficulties in clinical site initiation, including difficulties in recruiting clinical site investigators and clinical site staff;
- delays in clinical sites receiving the supplies and materials needed to conduct our clinical trials, including interruption in global shipping that may affect the transport of clinical trial materials;
- difficulties interpreting data from our clinical trials due to the possible effects of the infectious disease on patients;
- changes in local regulations as part of a response to the public health crisis which may require us to change the ways in which our clinical trials are conducted, which may result in unexpected costs, or to discontinue the clinical trials altogether;
- interruptions, difficulties or delays arising in our existing operations;
- diversion of healthcare resources away from the conduct of ongoing or future clinical trials, including the diversion of hospitals serving as our clinical trial sites and hospital staff supporting the conduct of our clinical trials;
- interruption of key clinical trial activities, such as clinical trial site monitoring, due to limitations on travel imposed or recommended by federal or state governments, employers and others, or interruption of clinical trial subject visits and study procedures, the occurrence of which could affect the integrity of clinical trial data;

- limitations in resources that would otherwise be focused on the conduct of our business, our preclinical studies or our clinical trials, including because of sickness or the desire to avoid contact with large groups of people or as a result of government-imposed “shelter in place” or similar working restrictions;
- interruption or delays in the operations of the FDA or other regulatory authorities, which may impact review and approval timelines;
- interruption in global freight and shipping that may affect the transport of clinical trial materials, such as investigational drug product to be used in our clinical trials;
- risks relating to potential disruptions of our contracted manufacturing operations as a result of any potential shut downs or other restrictions in operations due to impact from the public health crisis;
- changes in regulations as part of a response to the epidemic or pandemic which may require us to change the ways in which our clinical trials are to be conducted, or to discontinue the clinical trials altogether, or which may result in unexpected costs;
- delays in necessary interactions with regulators, ethics committees and other important agencies and contractors due to limitations in employee resources or forced furlough of government or contractor personnel;
- risk that participants enrolled in our clinical trials will acquire an infectious disease while the clinical trial is ongoing, which could impact the results of the clinical trial, including by increasing the number of observed adverse events; and
- refusal of the FDA to accept data from clinical trials in affected geographies outside of their respective jurisdictions.

These and other disruptions in our operations and the global economy could negatively impact our business, operating results and financial condition.

In addition, to the extent a health epidemic or pandemic adversely affects our business and results of operations, it may also have the effect of heightening many of the other risks and uncertainties described in this “Risk Factors” section.

We may seek orphan drug designation for our product candidates from the FDA and/or from the EMA in the future. However, we may be unsuccessful in obtaining or may be unable to maintain the benefits associated with orphan drug designation, including the potential for market exclusivity.

We may seek orphan drug designation for our product candidates in the future; however, we may be unsuccessful. Regulatory authorities in some jurisdictions, including the United States and the European Union (EU), may designate drugs for relatively small patient populations as orphan drugs. Under the U.S. Orphan Drug Act, the FDA may designate a drug as an orphan drug if it is a drug intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals annually 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. In the EU, the EMA’s Committee for Orphan Medicinal Products may grant orphan drug designation to promote the development of products that are intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition, provided that the condition is affecting not more than five in 10,000 persons in the EU or if, without incentives, it is unlikely that marketing of the drug in the EU would generate sufficient returns to justify the investment needed to develop the drug, and no satisfactory method of diagnosis, prevention or treatment of the condition exists (or, if such a method exists, the drug must be of significant benefit to patients). There can be no assurance that the FDA or EMA will grant orphan designation for any indication for which we apply, or that we will be able to maintain such designation.

In the United States, orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers. 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 orphan drug exclusivity, which precludes the EMA or the FDA from approving another marketing application for the same drug or biologic for that time period, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity or where the manufacturer is unable to assure sufficient product quantity. The applicable exclusivity period is ten years in Europe, but such exclusivity period can be reduced to six years if a product no longer meets the criteria for orphan designation or if the product is sufficiently profitable so that market exclusivity is no longer justified. Moreover, 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 if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition.

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. Even after an orphan drug is approved, the FDA or comparable foreign regulatory authority can subsequently approve the same active moiety in a new drug for the same condition if such regulatory authority concludes that the later drug is clinically superior if 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 later determines that the initial request for designation was materially defective.

In addition, orphan drug exclusivity does not prevent the FDA from approving competing drugs for the same or similar indication containing a different active ingredient. In addition, if a subsequent drug is approved for marketing for the same or a similar indication as any of our product candidates that receive marketing approval, we may face increased competition and lose market share regardless of orphan drug exclusivity. Orphan drug designation neither shortens the development time or regulatory review time of a drug nor gives the drug any advantage in the regulatory review or approval process.

A Fast Track designation by the FDA may not actually lead to a faster development or regulatory review or approval process.

We may seek Fast Track designation for some of our product candidates. If a product is intended for the treatment of a serious or life-threatening condition and the product demonstrates the potential to address unmet medical needs for this condition, the product candidate may be eligible for Fast Track designation. In March 2022, the FDA granted Fast Track designation to DT-216 for the treatment of FA. The benefits of Fast Track designation include more frequent meetings with FDA to discuss the drug's development plan and ensure collection of appropriate data needed to support drug approval, more frequent written communication from the FDA about such things as the design of the proposed clinical trials and use of biomarkers, eligibility for Accelerated Approval and Priority Review, if relevant criteria are met, and rolling review for its NDA. Even with the 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.

Any Breakthrough Therapy designation that we may receive from the FDA for our product candidates may not lead to a faster development or regulatory review or approval process, and it does not increase the likelihood that our product candidates will receive marketing approval.

We may seek 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. For drugs that have been designated as a Breakthrough Therapy, 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 a Breakthrough Therapy by the FDA are also eligible for 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. We cannot be sure that any evaluation we may make of our product candidates as qualifying for Breakthrough Therapy designation will meet the FDA's expectations. 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 drugs 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 a Breakthrough Therapy, 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.

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

The biotechnology and biopharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary and novel products and product candidates. Our competitors have developed, are developing or may develop products, product candidates and processes competitive with our product candidates. Any product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future. We believe that a significant number of products are currently under development, and may become commercially available in the future, for the treatment of repeat expansion driven diseases, including FA, FECD and DM1. Our competitors include larger and better funded pharmaceutical, specialty pharmaceutical and biotechnology companies. Moreover, we may also compete with universities, governmental agencies and other research institutions who may be active in the indications we are targeting and could be in direct competition with us. We also compete with these organizations in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies.

On February 28, 2023, Reata Pharmaceuticals announced that the FDA approved omaveloxolone a Nrf2 activator, for the treatment of FA in adults and adolescents aged 16 years and older. We are also aware of a number of companies with active clinical stage FA programs including (i) Larimar Therapeutics evaluating CTI-1601, a cell penetrating peptide FXN recombinant fusion protein, (ii) Lexeo Therapeutics evaluating a cardiac targeted FXN gene therapy, (iii) Minoryx Therapeutics evaluating leriglitazone, a PPAR-gamma agonist, and (iv) PTC Therapeutics evaluating vatiquinone, a 15-lipoxygenase inhibitor. In addition, several companies have stated that they have gene therapy programs for FA including Lacerta Therapeutics, Novartis, Pfizer, PTC Therapeutics, Solid Biosciences, StrideBio, and Voyager Therapeutics.

We are aware of a number of companies with active clinical stage FECD programs including (i) Aurion Biotech evaluating Vyznova, expanded donor cells for transplant, (ii) Emmecell evaluating donor cornea endothelial cells delivered through magnetic nanoparticles injected into the anterior chamber, (iii) Kowa Pharmaceutical evaluating Ripasudil, a Rho-kinase inhibitor, for use in conjunction with corneal surgery, (iv) Santen Pharmaceutical evaluating STN1010904, an mTOR inhibitor, and (v) Trefoil Therapeutics evaluating TTHX1114, an engineered FGF1 delivered via intracameral injection, for use in conjunction with corneal surgery.

We are aware of a number of programs for DM1 including (i) AMO Pharma evaluating tideglusib, a GSK3- β inhibitor, (ii) small molecules interacting with RNA under evaluation by Anima Biotech, (iii) anti-miRNA oligonucleotides under evaluation by Arthex Biotech, (iv) Astellas Pharma evaluating an AAV-antisense candidate, (v) Avidity Biosciences evaluating an antibody linked siRNA, (vi) Dyne Therapeutics evaluating an antibody linked oligonucleotide, (vii) Entrada Therapeutics evaluating a peptide conjugated oligonucleotide, (viii) an AAV-based RNA degrading gene therapy by Enzerna Biosciences, (ix) small molecules interacting with RNA under evaluation by Expansion Therapeutics, (x) Harmony Biosciences evaluating a histamine 3 receptor for the treatment of excessive daytime sleepiness in DM1, (xi) an RNA-targeting AAV-based gene therapy by Locanabio, (xii) PepGen evaluating a peptide conjugated antisense oligonucleotide, and (xiii) gene editing treatments by Vertex Pharmaceuticals.

We will also compete more generally with other companies developing alternative scientific and technological approaches to modulate individual genes, including other companies working to develop nuclease-based gene editing technologies, such as Beam Therapeutics, CRISPR Therapeutics, Editas Medicine, Intellia Therapeutics, Precision BioSciences and Sangamo Biosciences.

Many of our competitors, either alone or with their collaborators, have significantly greater financial, technical, manufacturing, marketing, sales and supply resources or experience than we do. 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 products we may develop. Competitive products may make any products we develop 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 we may develop, if approved, could be adversely affected.

Disruptions at the FDA and other government agencies caused by funding shortages or global health concerns could hinder their ability to hire and retain key leadership and other personnel, or otherwise prevent new products and services from being developed or commercialized in a timely manner, 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, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory, and policy changes. Average review times at the agency 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, 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. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

Separately, in response to the global COVID-19 pandemic, the FDA and regulatory authorities outside the United States adopted restrictions or other policy measures that diverted resources and delayed their attention to routine submissions. If a prolonged government shutdown occurs, or if global health concerns prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews, or other regulatory activities, it could significantly impact the ability of the FDA or other regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on 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 must prioritize our research programs and will need to focus our discovery and development on select product candidates and indications. Correctly prioritizing our research and development activities is particularly important for us due to the breadth of potential product candidates and indications that we believe could be pursued using our platform technologies. 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. 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 products. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may also 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.

We may not be successful in our efforts to identify or discover additional product candidates in the future.

Our research programs may initially show promise in identifying potential product candidates, yet fail to yield product candidates for clinical development for a number of reasons, including:

- our inability to design such product candidates with the properties that we desire; or
- potential product candidates may, on further study, be shown to have harmful side effects or other characteristics that indicate that they are unlikely to be products that will receive marketing approval and achieve market acceptance.

Research programs to identify new product candidates require substantial technical, financial and human resources. If we are unable to identify suitable additional candidates for preclinical and clinical development, our opportunities to successfully develop and commercialize therapeutic products will be limited.

Risks Related to Manufacturing, Commercialization and Reliance on Third Parties

We may rely on third parties to conduct, supervise, and monitor our ongoing and planned clinical trials and perform some of our research and preclinical studies. If these third parties do not satisfactorily carry out their contractual duties or fail to meet expected deadlines, our development programs may be delayed or subject to increased costs, each of which may have an adverse effect on our business and prospects.

We do not have the ability to conduct all aspects of our preclinical testing or clinical trials ourselves. As a result, we are and expect to remain dependent on third parties to conduct our preclinical studies, our ongoing Phase 1 clinical trial and any future clinical trials of our product candidates. The timing of the initiation and completion of these studies and trials will therefore be partially controlled by such third parties and may result in delays to our development programs. Nevertheless, we are responsible for ensuring that each of our preclinical studies and ongoing and planned clinical trials is conducted in accordance with the applicable protocol, legal requirements, and scientific standards, and our reliance on the CROs and other third parties does not relieve us of our regulatory responsibilities. We and our CROs are required to comply with Good Laboratory Practice (GLP) and GCP requirements, which are regulations and guidelines enforced by the FDA, the Competent Authorities of the Member States of the European Economic Area, and comparable foreign regulatory authorities for all of our product candidates in clinical development. Regulatory authorities enforce these GLP and GCP requirements through periodic inspections of preclinical study sites, trial sponsors, clinical trial investigators and clinical trial sites. If we or any of our CROs or clinical trial sites fail to comply with applicable GLP or GCP requirements, the data generated in our preclinical studies and clinical trials may be deemed unreliable, and the FDA or comparable foreign regulatory authorities may require us to perform additional preclinical or clinical trials before approving our marketing applications. In addition, our clinical trials must be conducted with product produced under current Good Manufacturing Practice (cGMP) regulations. Our failure to comply with these regulations may require us to stop and/or repeat clinical trials, which would delay the marketing approval process.

There is no guarantee that any such CROs, clinical trial investigators or other third parties on which we rely will devote adequate time and resources to our development activities, provide services in a timely manner or perform as contractually required. These risks may be heightened as a result of the efforts of government agencies and the CROs themselves to limit the spread of COVID-19 or other infectious disease, including quarantines and shelter-in-place orders, which have adversely impacted the supply chain for many research and clinical supplies, including animals for preclinical testing. In addition, demand for CROs and their resources and services has increased in recent years, which has impacted performance timelines. Furthermore, there are shortages in the supply of materials and animal availability for preclinical testing, which are required to conduct preclinical studies. This has led us to experience increased competition for CRO services, including, without limitation, scheduling preclinical studies and delays in study reporting, which could impact development timelines. If any of these third parties fail to meet expected deadlines, adhere to our clinical protocols or meet regulatory requirements, otherwise performs in a substandard manner, or terminates its engagement with us, the timelines for our development programs may be extended or delayed or our development activities may be suspended or terminated. If any of our clinical trial sites terminates for any reason, we may experience the loss of follow-up information on subjects enrolled in such clinical trials unless we are able to transfer those subjects to another qualified clinical trial site, which may be difficult or impossible. In addition, clinical trial investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and may receive cash or equity compensation in connection with such services. If these relationships and any related compensation result in perceived or actual conflicts of interest, or the FDA or any comparable foreign regulatory authority concludes that the financial relationship may have affected the interpretation of the trial, the integrity of the data generated at the applicable clinical trial site may be questioned and the utility of the clinical trial itself may be jeopardized, which could result in the delay or rejection of any marketing application we submit by the FDA or any comparable foreign regulatory authority. Any such delay or rejection could prevent us from commercializing our product candidates.

Furthermore, these third parties may also have relationships with other entities, some of which may be our competitors. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we will not be able to obtain, or may be delayed in obtaining, marketing approvals for our product candidates and will not be able to, or may be delayed in our efforts to, successfully commercialize our products.

We contract with third parties for the manufacturing and supply of our product candidates for use in preclinical testing and clinical trials, which supply may become limited or interrupted or may not be of satisfactory quality and quantity.

We do not have any manufacturing facilities. We rely on third parties for the manufacture of our product candidates for preclinical and clinical testing. We will continue to rely on such third parties for commercial product manufacture, if any of our product candidates are approved. We currently have limited manufacturing arrangements and expect that each of our product candidates will only be covered by single source suppliers for the foreseeable future. This reliance increases the risk that we will not have sufficient quantities of our product candidates or products, if approved, or such quantities at an acceptable cost or quality, which could delay, prevent or impair our development or commercialization efforts.

Furthermore, all entities involved in the preparation of therapeutics for clinical trials or commercial sale, including our existing contract manufacturers for our product candidates, are subject to extensive regulation. Components of a finished therapeutic product approved for commercial sale or used in clinical trials must be manufactured in accordance with cGMP requirements. 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 contaminants, or to inadvertent changes in the properties or stability of our product candidates that may not be detectable in final product testing. We or our contract manufacturers must supply all necessary documentation in support of an NDA on a timely basis and must adhere to the FDA's cGMP regulations enforced by the FDA through its facilities inspection program. Comparable foreign regulatory authorities may require compliance with similar requirements. The facilities and quality systems of our third-party contract manufacturers must pass a pre-approval inspection for compliance with the applicable regulations as a condition of marketing approval of our product candidates. We do not have direct control of the manufacturing activities of, and are completely dependent on, our contract manufacturers for compliance with cGMP regulations.

In the event that any of our manufacturers fails to comply with such requirements or to perform its obligations to us in relation to quality, timing or otherwise, or if our supply of components or other materials becomes limited or interrupted for other reasons, including due to global supply chain challenges, geopolitical events impacting trade with global partners, labor shortages, or the resurgence of COVID-19 or other health epidemic or pandemic, we may be forced to manufacture the materials ourselves, for which we currently do not have the capabilities or resources, or enter into an agreement with another third-party, which we may not be able to do on commercially reasonable terms, if at all. In particular, any replacement of our manufacturers could require significant effort and expertise because there may be a limited number of qualified replacements. In some cases, the technical skills or technology required to manufacture our product candidates may be unique or proprietary to the original manufacturer and we may have difficulty transferring such skills or technology to another third-party and a feasible alternative may not exist. These factors would increase our reliance on such manufacturer or require us to obtain a license from such manufacturer in order to have another third-party manufacture our product candidates. If we are required to or voluntarily change manufacturers for any reason, we will be required to verify that the new manufacturer maintains facilities and procedures that comply with quality standards and with all applicable regulations and guidelines and that the product produced is equivalent to that produced in a prior facility. The delays associated with the verification of a new manufacturer and equivalent product could negatively affect our ability to develop product candidates in a timely manner or within budget.

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

- inability to meet our product specifications and quality requirements consistently;
- an inability to initiate or continue preclinical studies or clinical trials of our product candidates under development;
- delay in submitting regulatory applications, or receiving marketing approvals, for our product candidates, if at all;

- loss of the cooperation of future collaborators;
- subjecting third-party manufacturing facilities or our manufacturing facilities to additional inspections by regulatory authorities;
- requirements to cease development or to recall batches of our product candidates; and
- in the event of approval to market and commercialize our product candidates, an inability to meet commercial demands for any such products.

Changes in methods of product candidate manufacturing may result in additional costs or delays.

As product candidates progress through preclinical to late-stage clinical trials to marketing approval and commercialization, it is common that various aspects of the development program, such as manufacturing methods, are altered along the way in an effort to optimize yield, manufacture batch size, change drug product dosage form, minimize costs and achieve consistent quality and results. Such changes carry the risk that they will not achieve these intended objectives. Any of these changes could cause our product candidates to perform differently and affect the results of ongoing or planned clinical trials or other future clinical trials conducted with the altered materials. This could delay completion of clinical trials, require the conduct of bridging clinical trials or the repetition of one or more clinical trials, increase clinical trial costs, delay approval of our product candidates and jeopardize our ability to commercialize our product candidates and generate revenue.

Any approved products may fail to achieve the degree of market acceptance by physicians, patients, hospitals, healthcare payors and others in the medical community necessary for commercial success.

If any of our product candidates receive marketing approval, they may nonetheless fail to gain sufficient market acceptance by physicians, patients, healthcare payors and others in the medical community. Most of our product candidates target mechanisms for which there are limited or no currently approved products, which may result in slower adoption by physicians, patients and payors. If our product candidates do not achieve an adequate level of acceptance, we may not generate significant product revenue 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:

- efficacy and potential advantages compared to alternative treatments;
- our ability to offer our products for sale at competitive prices;
- 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 availability of coverage and adequate reimbursement from third-party payor programs, and the willingness of patients to pay out of pocket in the absence of such third-party payor coverage and reimbursement;
- the strength of marketing and distribution support; and
- the prevalence and severity of any side effects.

We may not be able to successfully commercialize our product candidates, if approved, due to unfavorable pricing regulations or third-party coverage and reimbursement policies, which could make it difficult for us to sell our product candidates profitably.

Obtaining coverage and reimbursement approval for a product from a government or other third-party payor is a time-consuming and costly process, with uncertain results, that could require us to provide supporting scientific, clinical and cost effectiveness data for the use of our products to the payor. There may be significant delays in obtaining such coverage and reimbursement for newly approved products, and coverage may not be available, or may be more limited than the purposes for which the product is approved by the FDA or comparable foreign regulatory authorities. Moreover, eligibility for coverage and reimbursement does not imply that a product will be paid for in all cases or at a rate that covers our costs, including research, development, intellectual property, manufacture, sale and distribution expenses. Interim reimbursement levels for new products, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the product and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost products and may be incorporated into existing payments for other services. Net prices for products may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors, by any future laws limiting drug prices and by any future relaxation of laws that presently restrict imports of product from countries where they may be sold at lower prices than in the United States.

There is significant uncertainty related to the insurance coverage and reimbursement of newly approved products. In the United States, there is no uniform policy among third-party payors for coverage and reimbursement. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting reimbursement policies, but also have their own methods and approval process apart from Medicare coverage and reimbursement determinations. Therefore, a third-party payor's determination to provide coverage for a product does not assure that other payors will also provide coverage for the product.

Coverage and reimbursement by a third-party payor may depend upon a number of factors, including the third-party payor's determination that use of a 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.

We cannot be sure that reimbursement will be available for any product that we commercialize and, if coverage and reimbursement are available, what the level of reimbursement will be. Obtaining reimbursement for our products may be particularly difficult because of the higher prices often associated with branded therapeutics and therapeutics administered under the supervision of a physician. Our inability to promptly obtain coverage and adequate reimbursement rates from both government-funded and private payors for any approved products that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

Reimbursement may impact the demand for, and the price of, any product for which we obtain marketing approval. Even if we obtain coverage for a given product by a third-party payor, the resulting reimbursement payment rates may not be adequate or may require co-payments that patients find unacceptably high. Patients who are prescribed medications for the treatment of their conditions, and their prescribing physicians, generally rely on third-party payors to reimburse all or part of the costs associated with those medications. Patients are unlikely to use our products unless coverage is provided and reimbursement is adequate to cover all or a significant portion of the cost of our products. Therefore, coverage and adequate reimbursement are critical to a new product's acceptance. Coverage decisions may depend upon clinical and economic standards that disfavor new products when more established or lower cost therapeutic alternatives are already available or subsequently become available.

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 may or may not be available. Instead, the hospital or administering physician may be reimbursed only for providing the treatment or procedure in which our product is used. Further, from time to time, the Centers for Medicare & Medicaid Services (CMS) revises the reimbursement systems used to reimburse health care providers, including the Medicare Physician Fee Schedule and Hospital Outpatient Prospective Payment System, which may result in reduced Medicare payments.

We expect to experience pricing pressures in connection with the sale of any of our product candidates due to the trend toward managed healthcare, the increasing influence of health maintenance organizations, and additional legislative changes. The downward pressure on healthcare costs in general, particularly prescription medicines, medical devices and surgical procedures and other treatments, has become very intense. As a result, increasingly high barriers are being erected to the successful commercialization of new products. Further, the adoption and implementation of any future governmental cost containment or other health reform initiative may result in additional downward pressure on the price that we may receive for any approved product.

Additionally, we or collaborators may develop companion diagnostic tests for use with our product candidates. We, or our collaborators, will be required to obtain coverage and reimbursement for these tests separate and apart from the coverage and reimbursement we may seek for our product candidates. While we have not yet developed any companion diagnostic tests for our product candidates, if we do, there is significant uncertainty regarding our ability to obtain coverage and adequate reimbursement for the same reasons applicable to our product candidates.

Outside of the United States, many countries require approval of the sale price of a product before it can be marketed, and the pricing review period only begins after marketing or product licensing approval is granted. To obtain reimbursement or pricing approval in some of these countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidate to other available therapies. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a product candidate in a particular country, but then be subject to price regulations that delay our commercial launch of the product, possibly for lengthy time periods, and negatively impact the revenue, if any, we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if such product candidates obtain marketing approval.

If the market opportunities for any of our product candidates are smaller than we believe they are, our revenue may be adversely affected, and our business may suffer.

We are focused initially on the development of treatments for nucleotide expansion repeat diseases. Our projections of addressable patient populations that have the potential to benefit from treatment with our product candidates are based on estimates. If any of our estimates are inaccurate, the market opportunities for any of our product candidates could be significantly diminished and have an adverse material impact on our business.

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

Because we rely on third parties to research and develop and to manufacture our product candidates, we must share trade secrets with them. We seek to protect our proprietary technology in part by entering into confidentiality agreements and, if applicable, material transfer agreements, consulting agreements or other similar agreements with our advisors, employees, third-party contractors and consultants prior to beginning research or disclosing proprietary information. 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, are inadvertently incorporated into the technology of others, or are disclosed or used in violation of these agreements. Given that our proprietary position is based, in part, on our know-how and trade secrets, a competitor's independent discovery of our trade secrets or other unauthorized use or disclosure would impair our competitive position and may have a material adverse effect on our business.

In addition, these agreements typically restrict the ability of our advisors, employees, third-party contractors and consultants to publish data potentially relating to our trade secrets, although our agreements may contain certain limited publication rights. For example, any academic institution that we may collaborate with will likely expect to be granted rights to publish data arising out of such collaboration and any joint research and development programs may require us to share trade secrets under the terms of our research and development or similar agreements. Despite our efforts to protect our trade secrets, our competitors may discover our trade secrets, either through breach of our agreements with third parties, independent development or publication of information by any of our third-party collaborators. A competitor's discovery of our trade secrets would impair our competitive position and have an adverse impact on our business.

If any of our product candidates are approved for marketing and commercialization and we are unable to establish sales and marketing capabilities or enter into agreements with third parties to sell and market our product candidates, we will be unable to successfully commercialize our product candidates if and when they are approved.

We have no sales, marketing or distribution capabilities or experience. To achieve commercial success for any approved product for which we retain sales and marketing responsibilities, we must either develop a sales and marketing organization, which would be expensive and time consuming, or outsource these functions to other third parties. In the future, we may choose to build a focused sales and marketing infrastructure to sell, or participate in sales activities with our collaborators for, some of our product candidates if and when they are approved.

There are risks involved with both establishing our own sales and marketing capabilities and entering into arrangements with third parties to perform these services. 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. This 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 future products on our own include:

- our inability to recruit and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to physicians or educate adequate numbers of physicians on the benefits of prescribing any future products;
- 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 portfolios; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

If we enter into arrangements with third parties to perform sales, marketing and distribution services, our product revenue or the profitability of this product revenue to us are likely to be lower than if we were to market and sell any products that we develop ourselves. In addition, we may not be successful in entering into arrangements with third parties to sell and market our product candidates or may be unable to do so on terms that are favorable to us. In entering into third-party marketing or distribution arrangements, any revenue we receive will depend upon the efforts of the third parties and we cannot assure you that such third parties will establish adequate sales and distribution capabilities or devote the necessary resources and attention to sell and market any future products effectively. If we do not establish sales and marketing capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates.

Even if we obtain FDA approval of any of our product candidates, we may never obtain approval or commercialize such products outside of the United States, which would limit our ability to realize their full market potential.

In order to market any products outside of the United States, we must establish and comply with numerous and varying regulatory requirements of other countries regarding safety and efficacy. Clinical trials conducted in one country may not be accepted by regulatory authorities in other countries, and regulatory approval in one country does not mean that regulatory approval will be obtained in any other country. Approval procedures vary among countries and can involve additional product testing and validation and additional administrative review periods. Seeking foreign regulatory approvals could result in significant delays, difficulties and costs for us and may require additional preclinical studies or clinical trials which would be costly and time consuming. Regulatory requirements can vary widely from country to country and could delay or prevent the introduction of our products in those countries. Satisfying these and other regulatory requirements is costly, time consuming, uncertain and subject to unanticipated delays. In addition, our failure to obtain regulatory approval in any country may delay or have negative effects on the process for regulatory approval in other countries. We do not have any product candidates approved for sale in any jurisdiction, including international markets, and we do not have experience in obtaining regulatory approval in international markets. If we fail to comply with regulatory requirements in international markets or to obtain and maintain required approvals, our ability to realize the full market potential of our products will be harmed.

Risks Related to Our In-Licenses and Other Strategic Agreements

We may not realize the benefits of any acquisitions, in-license or strategic alliances that we enter into.

We have entered into in-license agreements with multiple licensors and in the future may seek and form strategic alliances, create joint ventures or collaborations, or enter into acquisitions or additional licensing arrangements with third parties that we believe will complement or augment our existing technologies and product candidates.

These transactions can entail numerous operational and financial risks, including exposure to unknown liabilities, disruption of our business and diversion of our management's time and attention in order to manage a collaboration or develop acquired products, product candidates or technologies, incurrence of substantial debt or dilutive issuances of equity securities to pay transaction consideration or costs, higher than expected collaboration, acquisition or integration costs, write-downs of assets or goodwill or impairment charges, increased amortization expenses, difficulty and cost in facilitating the collaboration or combining the operations and personnel of any acquired business, impairment of relationships with key suppliers, manufacturers or customers of any acquired business due to changes in management and ownership and the inability to retain key employees of any acquired business. As a result, if we enter into acquisition or in-license agreements or strategic partnerships, 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, or if there are materially adverse impacts on our or the counterparty's operations resulting from global supply chain challenges, labor shortages or a resurgence of COVID-19 or health epidemic or pandemic, which could delay our timelines or otherwise adversely affect our business. We also cannot be certain that, following a strategic transaction or license, we will achieve the revenue or specific net income that justifies such transaction or such other benefits that led us to enter into the arrangement.

We may wish to form collaborations in the future with respect to our product candidates, but may not be able to do so or to realize the potential benefits of such transactions, which may cause us to alter or delay our development and commercialization plans.

The development and potential commercialization of our product candidates will require substantial additional capital to fund expenses. We may, in the future, decide to collaborate with other biopharmaceutical companies for the development and potential commercialization of those product candidates, including in territories outside the United States or for certain indications. We will face significant competition in seeking appropriate collaborators. We may not be successful in our efforts to establish a strategic partnership or other alternative arrangements for our product candidates because they may be deemed to be at too early of a stage of development for collaborative effort and third parties may not view our product candidates as having the requisite potential to demonstrate safety and efficacy. If and when we collaborate with a third-party for development and commercialization of a product candidate, we can expect to relinquish some or all of the control over the future success of that product candidate to the third-party. Our ability to 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 our technologies, product candidates and market opportunities. 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 for our product candidate. We may also be restricted under any license agreements from entering into agreements on certain terms or at all with potential collaborators.

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 and changes to the strategies of the combined company. As a result, 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 such product candidate, reduce or delay one or more of our other development programs, delay the potential commercialization or reduce the scope of any planned sales or marketing activities for such product candidate, or increase our expenditures and undertake development, manufacturing or commercialization activities at our own expense. If we elect to increase our expenditures to fund development, manufacturing or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop our product candidates or bring them to market and generate product revenue.

Our product candidates may also require specific technologies to work effectively and efficiently, and rights to those technologies may be held by others. We may be unable to in-license any compositions, methods of use, processes or other third party intellectual property rights from third parties that we identify. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, which would harm our business. Even if we are able to obtain a license, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. In that event, we may be required to expend significant time and resources to develop or license replacement technology.

Risks Related to Our Business Operations, Employee Matters and Managing Growth

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, principal investigators, consultants and commercial partners. Misconduct by these parties could include intentional failures to comply with the regulations of the FDA and non-U.S. regulators, provide accurate information to the FDA and non-U.S. regulators, 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 may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Such misconduct could also involve the improper use of information obtained in the course of clinical trials, 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 governmental 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 those actions could have a significant impact on our business, including the imposition of significant civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, exclusion from government funded healthcare programs, such as Medicare and Medicaid, contractual damages, reputational harm, diminished profits and future earnings, additional reporting obligations and oversight if subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with these laws, and the curtailment or restructuring of our operations.

We face potential product liability, and, if successful claims are brought against us, we may incur substantial liability and costs. If the use of our product candidates harms patients or is perceived to harm patients even when such harm is unrelated to our product candidates, our regulatory approvals could be revoked or otherwise negatively impacted and we could be subject to costly and damaging product liability claims.

The use of our product candidates in clinical trials and the sale of any products for which we obtain marketing approval exposes us to the risk of product liability claims. Product liability claims might be brought against us by consumers, healthcare providers, pharmaceutical companies or others selling or otherwise coming into contact with our products. There is a risk that our product candidates may induce adverse events. If we cannot successfully defend against product liability claims, we could incur substantial liability and costs. In addition, regardless of merit or eventual outcome, product liability claims may result in:

- impairment of our business reputation;
- withdrawal of clinical trial participants;
- costs due to related litigation;
- distraction of management's attention from our primary business;
- substantial monetary awards to patients or other claimants;
- the inability to commercialize our product candidates; and
- decreased demand for our product candidates, if approved for commercial sale.

We may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. If and when we obtain marketing approval for product candidates, we intend to expand our insurance coverage to include the sale of commercial products; however, we may be unable to obtain product liability insurance on commercially reasonable terms or in adequate amounts. On occasion, large judgments have been awarded in class action lawsuits based on drugs or medical treatments that had unanticipated adverse effects. A successful product liability claims, or series of claims brought against us could cause our stock price to decline and, if judgments exceed our insurance coverage, could adversely affect our results of operations and business.

We face an inherent risk of product liability as a result of the planned studies and ongoing clinical trials of our product candidates and will face an even greater risk if we commercialize our product candidates. For example, we may be sued if our product candidates allegedly cause injury or are found to be otherwise unsuitable during product testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product candidate, negligence, strict liability and a breach of warranties. Claims may be brought against us by clinical trial participants, patients or others using, administering or selling products that may be approved in the future. Claims could also be asserted under state consumer protection acts.

We are highly dependent on our key personnel, and if we are not successful in attracting and retaining highly qualified personnel, we may not be able to successfully implement our business strategy.

Our ability to compete in the highly competitive biotechnology and pharmaceutical industries depends upon our ability to attract and retain highly qualified managerial, scientific and medical personnel. We are highly dependent on our management, scientific and medical personnel. The loss of the services of any of our executive officers, other key employees, and other scientific and medical advisors, and our inability to find suitable replacements could result in delays in product development and harm our business.

We conduct substantially all of our operations at our leased laboratory and office space in Carlsbad, California and remotely. This region is headquarters to many other biopharmaceutical companies and many academic and research institutions. Competition for skilled personnel in our market is intense and may limit our ability to hire and retain highly qualified personnel on acceptable terms or at all.

To induce valuable employees to remain at our company, in addition to salary and cash incentives, we have provided stock options and restricted stock awards that vest over time. The value to employees of stock awards and restricted stock awards that vest over time may be significantly affected by movements in our stock price that are beyond our control and may at any time be insufficient to counteract more lucrative offers from other companies. Despite our efforts to retain valuable employees, members of our management, scientific and development teams may terminate their employment with us on short notice. Although we have employment agreements with certain of our key employees, these employment agreements provide for at-will employment, which means that any of our employees could leave our employment at any time, with or without notice. We do not maintain “key person” insurance policies on the lives of these individuals or the lives of any of our employees. Our success also depends on our ability to continue to attract, retain and motivate highly skilled junior, mid-level and senior managers as well as junior, mid-level and senior scientific and medical personnel.

We expect to expand our development, regulatory and operational 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 58 employees. In addition, we also utilize specialized contract research organizations for additional research and development personnel. Together with our employees, our team comprised approximately 132 full-time equivalents as of December 31, 2022. As we advance our research and development programs, we may be required to further increase the number of our employees and the scope of our operations, particularly in the areas of clinical development, discovery biology, chemistry, product development, general and administrative matters relating to being a public company, regulatory affairs and, if any of our product candidates receives marketing approval, sales, marketing and distribution. To manage any future growth, we must:

- identify, recruit integrate, maintain and motivate additional qualified personnel;

- manage our development efforts effectively, including the initiation and conduct of clinical trials for our product candidates; and
- improve our operational, financial and management controls, reporting systems and procedures.

Our future financial performance and our ability to develop, manufacture and commercialize our product candidates, if approved, will depend, in part, on our ability to effectively manage any future growth, and our management may also have to divert financial and other resources, and a disproportionate amount of its attention away from day-to-day activities in order to devote a substantial amount of time, to managing these growth activities.

If we are not able to effectively expand our organization by hiring new employees and expanding our groups of consultants and contractors, we may not be able to successfully implement the tasks necessary to further develop and commercialize our product candidates and, accordingly, may not achieve our research, development and commercialization goals.

Our ability to use our net operating loss carryforwards and certain other tax attributes may be limited.

We have incurred substantial losses during our history and do not expect to become profitable in the near future, and we may never achieve profitability. Under current law, U.S. federal net operating losses (NOLs), incurred in taxable years beginning after December 31, 2017, can be carried forward indefinitely to offset future taxable income, but the deductibility of such U.S. federal NOLs in taxable years beginning after December 31, 2020, is limited to 80% of taxable income. It is uncertain if and to what extent various states will conform to federal tax laws.

As of December 31, 2022, we had \$54.8 million of U.S. federal NOLs and \$10.6 million of state NOLs. U.S. federal NOL carryforwards totaling \$0.1 million will begin to expire in 2037 unless previously utilized, and U.S. federal NOL carryforwards of \$54.7 million generated after 2017 can be carried forward indefinitely under current law but can only be utilized to offset 80% of future taxable income. State NOL carryforwards totaling \$10.2 million will begin to expire in 2037, unless previously utilized. As of December 31, 2022, we also had aggregate U.S. federal and state research and development (R&D) credits of approximately \$3.1 million and \$1.4 million, respectively. U.S. federal R&D credits carryforwards begin to expire in 2038 unless previously utilized. The state R&D credit carryforwards do not expire. Our NOL carryforwards and R&D credits are subject to review and possible adjustment by the U.S. and state tax authorities.

In addition, under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, and corresponding provisions of state law, if a corporation undergoes an “ownership change,” which is generally defined as a greater than 50 percentage point change (by value) in its equity ownership over a three-year period, the corporation’s ability to use its pre-change NOL carryforwards, R&D credits and certain other tax attributes to offset its post-change income or taxes may be limited. This could limit the amount of NOLs, R&D credit carryforwards or other applicable tax attributes that we can utilize annually to offset future taxable income or tax liabilities. Subsequent ownership changes and changes to the U.S. tax rules in respect of the utilization of NOLs, R&D credits and other applicable tax attributes carried forward may further affect the limitation in future years. In addition, at the state level, there may be periods during which the use of NOLs is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed. As a result, we may be unable to use all or a material portion of our NOL carryforwards and other tax attributes, which could adversely affect our future cash flows. We have completed a Section 382 study to assess whether an ownership change had occurred from our formation through December 31, 2021. Based upon the study, we determined that we experienced multiple ownership changes during 2020, causing the annual utilization of NOLs, R&D credits, and other applicable tax attributes generated before then to be limited. We do not believe any of the NOLs, R&D credits, and other applicable tax attributes generated through December 31, 2021 will expire solely as a result of the limitations caused by these ownership changes. We may experience additional ownership changes in the future as a result of subsequent shifts in our stock ownership. As a result, if we earn net taxable income, our ability to use our pre-change NOLs to offset U.S. federal taxable income may be subject to further limitations, which could potentially result in increased future tax liability to us.

Risks Related to Government Regulation

Our business operations and current and future relationships with investigators, health care professionals, consultants, third-party payors and customers are subject, directly or indirectly, to federal and state healthcare fraud and abuse laws, transparency laws and other healthcare laws and regulations. If we are unable to comply, or have not fully complied, with such laws, we could face substantial penalties.

Although we do not currently have any products on the market, our operations may be, directly or indirectly through our prescribers, customers and third-party payors, subject to various U.S. federal and state healthcare laws and regulations, including, without limitation, the U.S. federal Anti-Kickback Statute, the U.S. federal civil and criminal false claims laws and the Physician Payments Sunshine Act and regulations. Healthcare providers and others play a primary role in the recommendation and prescription of any products for which we obtain marketing approval. These laws may impact, among other things, our current business operations, including our clinical research activities, and proposed sales, marketing and education programs and constrain the business of financial arrangements and relationships with healthcare providers and other parties through which we may market, sell and distribute our products for which we obtain marketing approval. In addition, we may be subject to additional healthcare, statutory and regulatory requirements and enforcement by foreign regulatory authorities in jurisdictions in which we conduct our business. The laws that may affect our ability to operate include:

- the U.S. federal Anti-Kickback Statute, which prohibits, among other things, persons or entities from knowingly and willfully soliciting, offering, receiving or paying any remuneration (including any kickback, bribe or certain rebates), directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, lease, order or recommendation of, any good, facility, item or service, for which payment may be made, in whole or in part, under U.S. federal and state healthcare programs such as Medicare and Medicaid. 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. federal false claims, including the False Claims Act, which can be enforced through whistleblower actions, and civil monetary penalties laws, which, among other things, impose criminal and civil penalties against individuals or entities for knowingly presenting, or causing to be presented, to the U.S. federal government, claims for payment or approval that are false or fraudulent, knowingly making, using or causing to be made or used, a false record or statement material to a false or fraudulent claim, or from knowingly making a false statement to avoid, decrease or conceal an obligation to pay money to the U.S. federal government. In addition, the government may assert that a claim including items and services resulting from a violation of the U.S. federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act;
- the U.S. federal Health Insurance Portability and Accountability Act of 1996 (HIPAA) which imposes criminal and civil liability for, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, or knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement, in connection with the delivery of, or payment for, healthcare benefits, items or services; similar to the 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;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, and their respective implementing regulations, impose requirements on certain covered healthcare providers, health plans, and healthcare clearinghouses as well as their respective business associates and their covered subcontractors that perform services for them that involve the use, or disclosure of, individually identifiable health information, relating to the privacy, security, and transmission of such individually identifiable health information;
- the U.S. Federal Food, Drug and Cosmetic Act, which prohibits, among other things, the adulteration or misbranding of drugs, biologics and medical devices;

- the U.S. federal legislation commonly referred to as Physician Payments Sunshine Act, enacted as part of the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act (collectively, the Affordable Care 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 to report annually to CMS information related to certain payments and other transfers of value to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), other healthcare professionals (such as physician assistants and nurse practitioners) and teaching hospitals, as well as information regarding ownership and investment interests held by the physicians described above and their immediate family members.
- analogous state laws and regulations, including: state anti-kickback and false claims laws, which may apply to our business practices, including, but not limited to, research, distribution, sales and marketing arrangements and claims involving healthcare items or services reimbursed by any third-party payor, including private insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry’s voluntary compliance guidelines and the relevant compliance guidance promulgated by the U.S. federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state laws and regulations that require drug manufacturers to file reports relating to pricing and marketing information, which requires tracking gifts and other remuneration and items of value provided to healthcare professionals and entities; and state and local laws requiring the registration of pharmaceutical sales representatives; and
- European and other foreign law equivalents of each of the laws, including reporting requirements detailing interactions with and payments to healthcare providers.

Ensuring that our internal operations and future business arrangements with third parties comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations, agency guidance or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of the laws described above or any other governmental laws and regulations that may apply to us, we may be subject to significant penalties, including civil, criminal and administrative penalties, damages, fines, exclusion from U.S. government funded healthcare programs, such as Medicare and Medicaid, or similar programs in other countries or jurisdictions, disgorgement, imprisonment, contractual damages, reputational harm, diminished profits, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws and the delay, reduction, termination or restructuring of our operations. 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 is found to not be in compliance with applicable laws, they may be subject to significant criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs and imprisonment. If any of the above occur, it could adversely affect our ability to operate our business and our results of operations.

Enacted and future legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates and affect the prices we may charge for such product candidates.

The United States and many foreign jurisdictions have enacted or proposed legislative and regulatory changes affecting the healthcare system that could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any product for which we obtain marketing approval.

In March 2010, the Affordable Care Act was enacted, which includes measures that have significantly changed the way health care is financed by both governmental and private insurers. There have been executive, judicial and congressional challenges to certain aspects of the Affordable Care Act. On June 17, 2021 the U.S. Supreme Court dismissed a challenge on procedural grounds that argued the Affordable Care Act is unconstitutional in its entirety because the “individual mandate” was repealed by Congress. However, it is possible that the Affordable Care Act will be subject to additional judicial or Congressional challenges in the future. Further, prior to the U.S. Supreme Court ruling, on January 28, 2021, President Biden issued an executive order that initiated a special enrollment period for purposes of obtaining health insurance coverage through the Affordable Care Act marketplace. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the Affordable Care Act. On August 16, 2022, President Biden signed the Inflation Reduction Act of 2022 (Inflation Reduction Act) into law, which among other things, extends enhanced subsidies for individuals purchasing health insurance coverage in Affordable Care Act marketplaces through plan year 2025. The Inflation Reduction Act also eliminates the "donut hole" under the Medicare Part D program beginning in 2025 by significantly lowering the beneficiary maximum out-of-pocket cost and through a newly established manufacturer discount program. It is unclear how any additional healthcare reform measures of the Biden administration will impact the Affordable Care Act or our business.

Other legislative changes have been proposed and adopted since the Affordable Care Act was enacted. For example, in August 2011, the Budget Control Act of 2011 was signed into law, which, among other things, included aggregate reductions to Medicare payments to providers of, on average, 2% per fiscal year, which, due to subsequent legislative amendments, including the Infrastructure Investment and Jobs Act, will stay in effect through 2031. However, COVID-19 relief legislation suspended the 2% Medicare sequester from May 1, 2020 through March 31, 2022. Following the resumption of the sequester, under current legislation the actual reduction in Medicare payments will vary from 1% in 2022 to up to 4% in the final fiscal year of this sequester.

Recently, there has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices. Specifically, there have been several recent U.S. congressional inquiries and legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs and reform government program reimbursement methodologies for drugs. At the federal level, in July 2021, the Biden administration released an executive order, "Promoting Competition in the American Economy," with multiple provisions aimed at prescription drugs. In response to Biden's executive order, on September 9, 2021, the Department of Health and Human Services (HHS) released a Comprehensive Plan for Addressing High Drug Prices that outlines principles for drug pricing reform and sets out a variety of potential legislative policies that Congress could pursue to advance these principles. In addition, the Inflation Reduction Act will, among other things, (i) direct HHS to negotiate the price of certain drugs and biologics covered under Medicare, and subject drug manufacturers to civil monetary penalties and a potential excise tax by offering a price that is not equal to or less than the negotiated “maximum fair price” under the law, and (ii) impose rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation. The Inflation Reduction Act permits HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years. These provisions will take effect progressively starting in fiscal year 2023, although they may be subject to legal challenges. It is currently unclear how the Inflation Reduction Act will be effectuated but is likely to have a significant impact on the pharmaceutical industry. Further, the Biden administration released an additional executive order on October 14, 2022, directing HHS to submit a report on how the Center for Medicare and Medicaid Innovation can be further leveraged to test models for lowering drug costs for Medicare and Medicaid beneficiaries. It is unclear whether this executive order or similar policy initiatives will be implemented in the future.

At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control costs pharmaceutical and biological products. Moreover, 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.

We expect that the healthcare reform measures that have been adopted, and that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any approved product and could seriously harm our future revenues. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our products.

We are subject to stringent and changing U.S. and foreign laws, regulations, rules, contractual obligations, policies and other obligations related to data privacy and security. Our actual or perceived failure to comply with such obligations could lead to regulatory investigations or actions, litigation, fines and penalties, disruptions of our business operations, reputational harm and other adverse business impacts.

In the ordinary course of business, we and our collaborators and third-party providers may collect, receive, store, process, generate, use, transfer, disclose, make accessible, protect, secure, dispose of, transmit, and share (collectively, processing) personal data and other sensitive information, such as proprietary and confidential business data, trade secrets, intellectual property, and data we collect about trial participants in connection with clinical trials. Our data processing activities may subject us to numerous data privacy and security obligations, such as various laws, regulations, guidance, industry standards, external and internal privacy and security policies, contracts, and other obligations that govern the processing of sensitive information by us and on our behalf. In the United States, federal, state, and local laws and regulations, including federal health information privacy laws, state data breach notification laws, state health information privacy laws and federal and state consumer protection laws (e.g., Section 5 of the Federal Trade Commission Act), govern the collection, use, disclosure and protection of health-related and other personal data and could apply to our operations or the operations of our collaborators and third-party providers. In addition, we may obtain health information from third parties (including research institutions from which we obtain clinical trial data) that are subject to privacy and security requirements under HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act ("HITECH"), which imposes specific requirements relating to the privacy, security, and transmission of individually identifiable health information. Depending on the facts and circumstances, we could be subject to significant penalties if we violate HIPAA.

States are also constantly amending existing laws, requiring attention to frequently changing regulatory requirements. For example, the California Consumer Privacy Act of 2018 (CCPA) imposes obligations on covered businesses. These obligations include, without limitation, providing specific disclosures in privacy notices and affording California residents certain rights related to their personal data. The CCPA allows for statutory fines for noncompliance (up to \$7,500 per violation) and a private right of action for certain data breaches. Although the CCPA exempts some data processed in the context of clinical trials, the CCPA may increase compliance costs and potential liability with respect to other personal data we may maintain about California residents. In addition, the California Privacy Rights Act of 2020 (CPRA), effective January 1, 2023, expands the CCPA, including by establishing a new California Privacy Protection Agency to implement and enforce the CPRA. At this time, we do not believe we are subject to the CCPA, as amended, but should we expand our operations in California, the CCPA will impose new and burdensome privacy compliance obligations on our business and will raise new risks for potential fines and class actions. Other states have also enacted data privacy laws, including Virginia, Colorado, Utah, and Connecticut, all of which differ from the CPRA and become effective in 2023. While these states, like the CCPA, also exempt some data processed in the context of clinical trials, these developments further complicate compliance efforts, and increase legal risk and compliance costs for us and the third parties upon whom we rely.

Outside the United States, an increasing number of laws, regulations, and industry standards apply to data privacy and security. For example, the European Union's General Data Protection Regulation (EU GDPR) and the United Kingdom's GDPR (UK GDPR) impose strict requirements for processing the personal data of individuals located, respectively, within the European Economic Area (EEA) and the United Kingdom (UK). For example, under the EU GDPR, companies may face temporary or definitive bans on data processing and other corrective actions; fines up to 20 million Euros or 4% of the annual global revenue, whichever is greater; or private litigation related to processing of personal data brought by classes of data subjects or consumer protection organizations authorized at law to represent their interests. The UK GDPR is independent from, but at present materially aligned with, the EU GDPR, which together with the UK Data Protection Act of 2018, covers the processing of personal information of individuals in the UK. Non-compliance with the UK GDPR may result in substantially similar adverse consequence to those in relation to the EU GDPR, including monetary penalties of up to £17.5 million or 4% of worldwide revenue, whichever is higher.

At this time, we do not believe we are subject to the EU GDPR or the UK GDPR, but should this change, the EU GDPR and the UK GDPR will increase our responsibility and potential liability in relation to personal data that we process, and we may be required to put in place additional mechanisms or change our business practices to ensure compliance with European and other foreign data protection rules.

Certain jurisdictions have enacted data localization laws and cross-border personal data transfers laws, which could make it more difficult to transfer information across jurisdictions (such as transferring or receiving personal data that originates in the EEA or in other foreign jurisdictions). Although there are currently various mechanisms that may be used to transfer personal data from the EU and UK to the United States in compliance with law, such as the EU and UK's standard contractual clauses, these mechanisms are subject to legal challenges, and there is no assurance that we can satisfy or rely on these measures to lawfully transfer personal data to the United States. If there is no lawful manner for us to transfer personal data from the EEA, the UK or other jurisdictions to the United States, or if the requirements for a legally-compliant transfer are too onerous, we could face significant adverse consequences, including the interruption or degradation of our operations, the need to relocate part of or all of our business or data processing activities to other jurisdictions at significant expense, increased exposure to regulatory actions, substantial fines and penalties, the inability to transfer data and work with partners, vendors and other third parties, and injunctions against our processing or transferring of personal data necessary to operate our business. Additionally, companies that transfer personal data out of the EEA and UK to other jurisdictions, particularly to the United States, are subject to increased scrutiny from regulators, individual litigants, and activist groups. Some European regulators have ordered certain companies to suspend or permanently cease certain transfers out of Europe for allegedly violating the GDPR's cross-border data transfer limitations.

In addition to data privacy and security laws we may be contractually subject to data privacy and security obligations, including industry standards adopted by industry groups and may become subject to new data privacy and security obligations in the future. For example, certain privacy laws, such as the GDPR and the CCPA, require customers to impose specific contractual restrictions on their service providers. We may also publish privacy policies, marketing materials and other statements, such as compliance with certain certifications or self-regulatory principles, regarding data privacy and security. If these policies, materials or statements are found to be deficient, lacking in transparency, deceptive, unfair, or misrepresentative of our practices, we may be subject to investigation, enforcement actions by regulators or other adverse consequences.

Obligations related to data privacy and security are quickly changing in an increasingly stringent fashion, creating some uncertainty as to the effective future legal framework. Additionally, these obligations may be subject to differing applications and interpretations, which may be inconsistent or conflict among jurisdictions. Preparing for and complying with these obligations requires significant resources and may necessitate changes to our information technologies, systems, and practices and to those of any third parties that process personal data on our behalf. In addition, these obligations may even require us to change our business model. Although we endeavor to comply with all applicable data privacy and security obligations, we may at times fail (or be perceived to have failed) to do so. Moreover, despite our efforts, our personnel or third-parties upon whom we rely may fail to comply with such obligations which could negatively impact our business operations and compliance posture. If we fail, or are perceived to have failed, to address or comply with data privacy and security obligations, we could face significant consequences. These consequences may include, but are not limited to, government enforcement actions (e.g., investigations, fines, penalties, audits, inspections and similar); litigation (including class-related claims); additional reporting requirements and/or oversight; bans on processing personal data; orders to destroy or not use personal data; and imprisonment of company officials. Any of these events could have a material adverse effect on our reputation, business, or financial condition, including but not limited to: loss of customers; interruptions or stoppages in our business operations (including, as relevant, clinical trials); inability to process personal data or operate in certain jurisdictions; limited ability to develop or commercialize our products; expenditure of time and resources to defend any claim or inquiry; adverse publicity; or revision or restructuring our operations.

Our business could be negatively impacted by environmental, social and corporate governance (ESG) matters or our reporting of such matters.

There is an increasing focus from certain investors, employees, partners, and other stakeholders concerning ESG matters. We may be, or be perceived to be, not acting responsibly in connection with these matters, which could negatively impact us. Moreover, the SEC has recently proposed, and may continue to propose, certain mandated ESG reporting requirements, such as the SEC's proposed rules to enhance and standardize climate-related disclosures, which, if approved, would significantly increase our compliance and reporting costs and may also result in disclosures that certain investors or other stakeholders do not favor which may negatively impact our reputation and/or harm our stock price. We currently do not report our environmental emissions and absent a legal requirement to do so we currently do not plan to report our environmental emissions, and lack of reporting could result in certain investors declining to invest in our common stock.

Risks Related to Our Intellectual Property

If we are unable to obtain and maintain sufficient intellectual property protection for our platform technologies and product candidates, or if the scope of the intellectual property protection is not sufficiently broad, our competitors could develop and commercialize products similar or identical to ours, and our ability to successfully commercialize our products may be adversely affected.

We rely upon a combination of patents, know-how, trade secrets, and confidentiality agreements to protect the intellectual property related to our products and technologies and to prevent third parties from copying and surpassing our achievements, thus eroding our competitive position in our market.

Our success depends in large part on our ability to obtain and maintain patent protection for our platform technologies, product candidates and their uses, as well as our ability to operate without infringing the proprietary rights of others. We seek to protect our proprietary position by filing patent applications in the United States and abroad related to our novel discoveries and technologies that are important to our business. Our pending and future patent applications may not result in patents being issued or provide assurance that issued patents will afford sufficient protection of our product candidates or their intended uses against competitors, nor can there be any assurance that the patents issued will not be infringed, designed around, invalidated by third parties, or effectively prevent others from commercializing competitive technologies, products or product candidates.

Obtaining and enforcing patents is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications or maintain and/or enforce patents that may issue based on our patent applications, at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development results before it is too late to obtain patent protection. Although we enter into non-disclosure and confidentiality agreements with parties who have access to patentable aspects of our research and development output, such as our employees, corporate collaborators, outside scientific collaborators, contract research organizations, contract manufacturers, consultants, advisors and other third parties, any of these parties may breach these agreements and disclose such results before a patent application is filed, thereby jeopardizing our ability to seek patent protection.

Composition of matter patents for biological and pharmaceutical product candidates often provide a strong form of intellectual property protection for those types of products, as such patents provide protection without regard to any method of use. We cannot be certain that the claims in our pending patent applications directed to composition of matter of our product candidates will be considered patentable by the United States Patent and Trademark Office (USPTO) or by patent offices in foreign countries, or that the claims in any of our issued patents will be considered valid and enforceable by courts in the United States or foreign countries. Method of use patents protect the use of a product for the specified method. This type of patent does not prevent a competitor from making and marketing a product that is identical to our product for an indication that is outside the scope of the patented method. Moreover, even if competitors do not actively promote their product for our targeted indications, physicians may prescribe these products “off-label.” Although off-label prescriptions may infringe or contribute to the infringement of method of use patents, the practice is common and such infringement is difficult to prevent or prosecute.

The patent position of biopharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation, resulting in court decisions, including Supreme Court decisions, which have increased uncertainties as to the ability to enforce patent rights in the future. In addition, the laws of foreign countries may not protect our rights to the same extent as the laws of the United States, or vice versa.

The patent application process is subject to numerous risks and uncertainties, and there can be no assurance that we or any of our potential future collaborators will be successful in protecting our product candidates by obtaining and defending patents. For example, we may not be aware of all third-party intellectual property rights potentially relating to our product candidates or their intended uses, and as a result the impact of such third-party intellectual property rights upon the patentability of our own patents and patent applications, as well as the impact of such third-party intellectual property upon our freedom to operate, is highly uncertain. 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 with certainty whether we were the first to make the inventions claimed in our patents or pending patent applications, or that we were the first to file for patent protection of such inventions. As a result, the issuance, inventorship, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending patent applications may be challenged in patent offices in the United States and abroad. Even issued patents may later be found invalid or unenforceable or may be modified or revoked in proceedings instituted by third parties before various patent offices or in courts. For example, our pending patent applications may be subject to third-party pre-issuance submissions of prior art to the USPTO or our issued patents may be subject to post-grant review (PGR) proceedings, oppositions, derivations, reexaminations, or inter partes review (IPR) proceedings, in the United States or elsewhere, challenging our patent rights or the patent rights of others. An adverse determination in any such challenges may result in loss of exclusivity or in patent claims being narrowed, invalidated, or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and products. In addition, given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. The degree of future protection for our proprietary rights is uncertain. Only limited protection may be available and may not adequately protect our rights or permit us to gain or keep any competitive advantage. Any failure to obtain or maintain patent protection with respect to our product candidates or their uses could have a material adverse effect on our business, financial condition, results of operations and prospects.

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, processes for which patents are difficult to enforce and any other elements of our discovery and development processes that involve proprietary know-how, information or technology that is not covered by patents. We may also rely on trade secret protection as temporary protection for concepts that may be included in a future patent filing. However, trade secret protection will not protect us from innovations that a competitor develops independently of our proprietary know-how. If a competitor independently develops a technology that we protect as a trade secret and files a patent application on that technology, then we may not be able to patent that technology in the future, may require a license from the competitor to use our own know-how, and if the license is not available on commercially-viable terms, then we may not be able to launch our product. Although we require all of our employees to assign their inventions to us, and require all of our employees, consultants, advisors and any third parties who have access to our proprietary know-how, information or technology to enter into confidentiality agreements, we cannot be certain that our trade secrets and other confidential proprietary information will not be disclosed or that competitors will not otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques. Furthermore, the laws of some foreign countries do not protect proprietary rights to the same extent or in the same manner as the laws of the United States. As a result, we may encounter significant problems in protecting and defending our intellectual property both in the United States and abroad. If we are unable to prevent unauthorized material disclosure of our intellectual property to third parties, we will not be able to establish or maintain a competitive advantage in our market, and this scenario could materially adversely affect our business, financial condition and results of operations.

We cannot ensure that patent rights relating to inventions described and claimed in our pending patent applications will issue or that patents based on our patent applications will not be challenged and rendered invalid and/or unenforceable.

The patent application process is subject to numerous risks and uncertainties, and there can be no assurance that we or any of our potential future collaborators will be successful in protecting our product candidates by obtaining and defending patents. We have pending U.S. and foreign patent applications in our portfolio; however, we cannot predict:

- if and when patents may issue based on our patent applications;
- the scope of protection of any patent issuing based on our patent applications;
- whether the claims of any patent issuing based on our patent applications will provide protection against competitors;
- whether or not third parties will find ways to invalidate or circumvent our patent rights;
- whether or not others will obtain patents claiming aspects similar to those covered by our patents and patent applications;
- whether we will need to initiate litigation or administrative proceedings to enforce and/or defend our patent rights which will be costly whether we win or lose;
- whether the patent applications that we own or in-license will result in issued patents with claims that cover our product candidates or uses thereof in the United States or in other foreign countries; and/or
- whether we may experience patent office interruption or delays to our ability to timely secure patent coverage to our product candidates as a result of factors outside our control.

We cannot be certain that the claims in our pending patent applications directed to our product candidates and/or technologies will be considered patentable by the USPTO or by patent offices in foreign countries. There can be no assurance that any such patent applications will issue as granted patents. One aspect of the determination of patentability of our inventions depends on the scope and content of the “prior art,” information that was or is deemed available to a person of skill in the relevant art prior to the priority date of the claimed invention. There may be prior art of which we are not aware that may affect the patentability of our patent claims or, if issued, affect the validity or enforceability of a patent claim. Even if the patents do issue based on our patent applications, third parties may challenge the validity, enforceability or scope thereof, which may result in such patents being narrowed, invalidated or held unenforceable. Furthermore, even if they are unchallenged, patents in our portfolio may not adequately exclude third parties from practicing relevant technology or prevent others from designing around our claims. If the breadth or strength of our intellectual property position with respect to our product candidates is threatened, it could dissuade companies from collaborating with us to develop and threaten our ability to commercialize our product candidates. In the event of litigation or administrative proceedings, we cannot be certain that the claims in any of our issued patents will be considered valid by courts in the United States or foreign countries.

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

Patents are of national or regional effect, and although we currently have an issued patent and pending applications in the United States, filing, prosecuting and defending patents on all of our research programs and product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection, but enforcement is not as strong as that in the United States. These competitor products may compete with our product candidates, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Various companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of many countries do not favor the enforcement of patents and other intellectual property protection, particularly those relating to pharmaceuticals, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights. In Europe, no earlier than October 1, 2022, European applications will soon have the option, upon grant of a patent, of becoming a Unitary Patent which will be subject to the jurisdiction of the Unitary Patent Court (UPC). This will be a significant change in European patent practice. As the UPC is a new court system, there is no precedent for the court, increasing the uncertainty.

Various countries outside the United States have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, many countries limit the enforceability of patents against government agencies or government contractors. As a result, a patent owner may have limited remedies in certain circumstances, which could materially diminish the value of such patent. If we are 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. 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.

Geopolitical actions in the United States and in foreign countries could increase the uncertainties and costs surrounding the prosecution or maintenance of our patent applications or those of any current or future licensors and the maintenance, enforcement or defense of our issued patents or those of any current or future licensors. For example, the United States and foreign government actions related to Russia’s invasion of Ukraine may limit or prevent filing, prosecution and maintenance of patent applications in Russia. Government actions may also prevent maintenance of issued patents in Russia. These actions could result in abandonment or lapse of our patents or patent applications, resulting in partial or complete loss of patent rights in Russia.

Further, the standards applied by the USPTO and foreign patent offices in granting patents are not always applied uniformly or predictably. As such, we do not know the degree of future protection that we will have on our technologies, products and product candidates. While we will endeavor to try to protect our technologies, products and product candidates with intellectual property rights such as patents, as appropriate, the process of obtaining patents is time consuming, expensive and unpredictable.

Changes in patent law in the United States and other jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our product candidates.

As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involves both technological and legal complexity and is therefore costly, time consuming and inherently uncertain. Changes in either the patent laws or interpretation of the patent laws in the United States could increase the uncertainties and costs, and may diminish our ability to protect our inventions, obtain, maintain, and enforce our intellectual property rights and, more generally, could affect the value of our intellectual property or narrow the scope of our owned and licensed patents. Patent reform legislation in the United States and other countries, including the Leahy-Smith America Invents Act (the Leahy-Smith Act), signed into law on September 16, 2011, could increase those uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents. The Leahy-Smith Act includes a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications are prosecuted, redefine prior art and provide more efficient and cost-effective avenues for competitors to challenge the validity of patents. 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. Further, because of a lower evidentiary standard in these USPTO post-grant 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 invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action. Accordingly, a third party may attempt to use the USPTO procedures to invalidate our patent claims that would not have been invalidated if first challenged by the third party as a defendant in a district court action. Thus, 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 issued patents, all of which could have a material adverse effect on our business, financial condition, results of operations and prospects.

After March 2013, under the Leahy-Smith Act, the United States transitioned to a first inventor to file system in which, assuming that the other statutory requirements 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. A third party that files a patent application in the USPTO after March 2013, but before we file an application covering the same invention, could therefore be awarded a patent covering an invention of ours even if we had made the invention before it was made by such third party. This will require us to be cognizant going forward of the time from invention to filing of a patent application. 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 and other proprietary technologies we may develop or (ii) invent any of the inventions claimed in our or our licensor's patents or patent applications. Even where we have a valid and enforceable patent, we may not be able to exclude others from practicing the claimed invention where the other party can show that they used the invention in commerce before our filing date or the other party benefits from a compulsory license. However, 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 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. The U.S. Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. Depending on future actions by the U.S. Congress, the U.S. courts, the USPTO and the relevant law-making bodies in other countries, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future. For example, in the 2013 case *Assoc. for Molecular Pathology v. Myriad Genetics, Inc.*, the U.S. Supreme Court held that certain claims to DNA molecules are not patentable. While we do not believe that any of the patents owned or licensed by us will be found invalid based on this decision, we cannot predict how future decisions by the courts, the U.S. Congress or the USPTO may impact the value of our patents.

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

Periodic maintenance fees, renewal fees, annuities fees and various other governmental fees on patents and/or patent applications are due to be paid to the USPTO and foreign patent agencies in several stages over the lifetime of the patent and/or patent application. The USPTO and various foreign governmental patent agencies also require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. If we fail to maintain the patents and patent applications covering our product candidates, our competitive position would be adversely affected.

Intellectual property rights do not necessarily address all potential threats to our competitive advantage.

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 product candidates that are similar to ours but that are not covered by the claims of the patents that we own or have exclusively licensed;
- we or our licensors 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 have exclusively licensed;
- we or our licensors or future collaborators might not have been the first to file patent applications covering certain of our inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights;
- it is possible that noncompliance with the USPTO and foreign governmental patent agencies requirement for a number of procedural, documentary, fee payment and other provisions during the patent process can result in abandonment or lapse of a patent or patent application, and partial or complete loss of patent rights in the relevant jurisdiction;
- it is possible that our pending patent applications will not lead to issued patents;
- issued patents that we own or have exclusively licensed may be revoked, modified, or held invalid or unenforceable, as a result of legal challenges by our competitors;

- our competitors might conduct research and development activities in countries where we do not have patent 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;
- we cannot predict the scope of protection of any patent issuing based on our patent applications, including whether the patent applications that we own or in-license will result in issued patents with claims that directed to our product candidates or uses thereof in the United States or in other foreign countries;
- there may be significant pressure on the U.S. government and international governmental bodies to limit the scope of patent protection both inside and outside the United States for disease treatments that prove successful, as a matter of public policy regarding worldwide health concerns;
- countries other than the United States may have patent laws less favorable to patentees than those upheld by U.S. courts, allowing foreign competitors a better opportunity to create, develop and market competing product candidates;
- the claims of any patent issuing based on our patent applications may not provide protection against competitors or any competitive advantages, or may be challenged by third parties;
- if enforced, a court may not hold that our patents are valid, enforceable and infringed;
- we may need to initiate litigation or administrative proceedings to enforce and/or defend our patent rights which will be costly whether we win or lose;
- we may choose not to file a patent application in order to maintain certain trade secrets or know-how, and a third party may subsequently file a patent application covering such intellectual property;
- we may fail to adequately protect and police our trademarks and trade secrets; and
- the patents of others may have an adverse effect on our business, including if others obtain patents claiming subject matter similar to or improving that covered by our patents and patent applications.

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

Our technology licensed from various third parties may be subject to retained rights.

We are currently party to a license agreement with WARF pursuant to which we acquired an exclusive license to certain patents relating to compounds and methods for modulating gene expression, compounds and methods for modulating FA expression and next generation synthetic transcription factors. WARF retains, and our future licensors may also retain, certain rights under the relevant agreements with us, including the right to use the underlying technology for noncommercial academic and research use, to publish general scientific findings from research related to the technology, and to make customary scientific and scholarly disclosures of information relating to the technology. It is difficult to monitor whether our licensors limit their use of the technology to these uses, and we could incur substantial expenses to enforce our rights to our licensed technology in the event of misuse.

In addition, the United States federal government retains certain rights in inventions produced with its financial assistance under the Patent and Trademark Law Amendments Act, or the Bayh-Dole Act. The federal government retains a “nonexclusive, nontransferable, irrevocable, paid-up license” for its own benefit. The Bayh-Dole Act also provides federal agencies with “march-in rights.” March-in rights allow the government, in specified circumstances, to require the contractor or successors in title to the patent to grant a “nonexclusive, partially exclusive, or exclusive license” to a “responsible applicant or applicants.” If the patent owner refuses to do so, the government may grant the license itself. We sometimes collaborate with academic institutions to accelerate our preclinical research or development. While it is our policy to avoid engaging our university partners in projects in which there is a risk that federal funds may be commingled, we cannot be sure that any co-developed intellectual property will be free from government rights pursuant to the Bayh-Dole Act. If, in the future, we co-own or license in technology which is critical to our business that is developed in whole or in part with federal funds subject to the Bayh-Dole Act, our ability to enforce or otherwise exploit patents covering such technology may be adversely affected.

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

Because our development programs may in the future require the use of proprietary rights held by third parties, the growth of our business may depend in part on our ability to acquire, in-license, or use these third-party proprietary rights. We may be unable to acquire or in-license any compositions, methods of use, processes or other third-party intellectual property rights from third parties that we identify as necessary for our product candidates. The licensing and acquisition of third-party intellectual property rights is a competitive area, and a number of 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 or at all. If we are unable to successfully obtain rights to required third-party intellectual property rights or maintain the existing intellectual property rights we have, we may have to abandon development of the relevant program or product candidate, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

While we normally seek to obtain the right to control prosecution, maintenance and enforcement of the patents relating to our product candidates, there may be times when the filing and prosecution activities for patents and patent applications relating to our product candidates are controlled by our future licensors or collaboration partners. If any of our future licensors or collaboration partners fail to prosecute, maintain and enforce such patents and patent applications in a manner consistent with the best interests of our business, including by payment of all applicable fees for patents covering our product candidates, we could lose our rights to the intellectual property or our exclusivity with respect to those rights, our ability to develop and commercialize those product candidates may be adversely affected and we may not be able to prevent competitors from making, using and selling competing products. In addition, even where we have the right to control patent prosecution of patents and patent applications we have licensed to and from third parties, we may still be adversely affected or prejudiced by actions or inactions of our licensees, our future licensors and their counsel that took place prior to the date upon which we assumed control over patent prosecution.

We may enter into license agreements in the future with others to advance our existing or future research or allow commercialization of our existing or future product candidates. These licenses may not provide exclusive rights to use such intellectual property and technology in all relevant fields of use and in all territories in which we may wish to develop or commercialize our technology and products in the future.

In addition, subject to the terms of any such license agreements, we may not have the right to control the preparation, filing, prosecution, maintenance, enforcement, and defense of patents and patent applications covering the technology that we license from third parties. In such an event, 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 future licensors fail to prosecute, maintain, enforce, and defend such patents or patent applications, or lose rights to those patents or patent applications, the rights we have licensed may be reduced or eliminated, and our right to develop and commercialize any of our product candidates that are subject of such licensed rights could be adversely affected.

Our future licensors may rely on third-party consultants or collaborators or on funds from third parties such that our future licensors are not the sole and exclusive owners of the patents we in-license. If other third parties have ownership rights to our future in-licensed patents, they may be able to license such patents to our competitors, and our competitors could market competing products and technology. This could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects.

It is possible that we may be unable to obtain licenses at a reasonable cost or on reasonable terms, if at all. Even if we are able to obtain a license, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. In that event, we may be required to expend significant time and resources to redesign our technology, 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 harm our business, financial condition, results of operations, and prospects significantly. We cannot provide any assurances that third-party patents do not exist which might be enforced against our current technology, manufacturing methods, product candidates, or future methods or products resulting in either an injunction prohibiting our manufacture or future sales, or, with respect to our future sales, an obligation on our part to pay royalties and/or other forms of compensation to third parties, which could be significant.

Disputes may arise between us and our future licensors regarding intellectual property subject to a license agreement, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- whether and the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- our right to sublicense patents and other rights to third parties;
- our diligence obligations under the license agreement and what activities satisfy those diligence obligations;
- our right to transfer or assign the license;
- the inventorship and ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our future licensors and us and our partners; and
- the priority of invention of patented technology.

In addition, the agreements under which we license intellectual property or technology from third parties are 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 financial or other obligations under the relevant agreement, either of which could have a material adverse effect on our business, financial condition, results of operations, and prospects. Moreover, if disputes over intellectual property that we license in the future prevent or impair our ability to maintain our licensing arrangements on commercially acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates, which could have a material adverse effect on our business, financial conditions, results of operations, and prospects.

In spite of our best efforts, our future licensors might conclude that we materially breached our license agreements and might therefore terminate the license agreements, thereby removing our ability to develop and commercialize products and technology covered by these license agreements. If these in-licenses are terminated, or if the underlying patents fail to provide the intended exclusivity, competitors would have the freedom to seek regulatory approval of, and to market, products identical to ours. This could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects.

From time to time, we may be required to license technologies relating to our therapeutic research programs from additional third parties to further develop or commercialize our product candidates. Should we be required to obtain licenses to any third-party technology, including any such patents required to manufacture, use or sell our product candidates, such licenses may not be available to us on commercially reasonable terms, or at all. The inability to obtain any third-party license required to develop or commercialize any of our product candidates could cause us to abandon any related efforts, which could seriously harm our business and operations.

Any future collaborations that we enter into may not be successful. The success of our collaboration arrangements will depend heavily on the efforts and activities of our collaborators. Collaborations are subject to numerous risks, which may include that:

- collaborators have significant discretion in determining the efforts and resources that they will apply to collaborations;
- collaborators may not pursue development and commercialization of our products or may elect not to continue or renew development or commercialization programs based on trial or test results, changes in their strategic focus due to the acquisition of competitive products, availability of funding or other external factors, such as a business combination that diverts resources or creates competing priorities;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our products or product candidates;
- a collaborator with marketing, manufacturing and distribution rights to one or more products may not commit sufficient resources to or otherwise not perform satisfactorily in carrying out these activities;
- we could grant exclusive rights to our collaborators that would prevent us from collaborating with others;
- collaborators may not properly maintain or defend our intellectual property rights or may use our intellectual property or proprietary information in a way that gives rise to actual or threatened litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential liability;
- disputes may arise between us and a collaborator that causes the delay or termination of the research, development or commercialization of our product candidates or that results in costly litigation or arbitration that diverts management attention and resources;
- collaborations may be terminated, and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates;
- collaborators may own or co-own intellectual property covering our products that results from our collaborating with them, and in such cases, we would not have the exclusive right to develop or commercialize such intellectual property; and
- a collaborator's sales and marketing activities or other operations may not be in compliance with applicable laws resulting in civil or criminal proceedings.

We may not identify relevant third-party patents or may incorrectly interpret the relevance, scope or expiration of a third-party patent, which might adversely affect our ability to develop and market our products.

As the biopharmaceutical industry expands and more patents are issued, the risk increases that our product candidates may be subject to claims of infringement of the patent rights of third parties. There can be no assurance that our operations do not, or will not in the future, infringe existing or future third-party patents. Identification of third-party patent rights that may be relevant to our operations is difficult 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 cannot guarantee that any of our patent searches or analyses, including the identification of relevant patents, the scope of patent claims or the expiration of relevant patents, are complete or thorough, nor can we be certain that we have identified each and every third-party patent and pending application in the United States and abroad that is relevant to or necessary for the commercialization of our product candidates in any jurisdiction.

Numerous U.S. and foreign patents and pending patent applications exist in our market that are owned by third parties. Our competitors in both the United States and abroad, many of which have substantially greater resources and have made substantial investments in patent portfolios and competing technologies, may have applied for or obtained or may in the future apply for and obtain, patents that will prevent, limit or otherwise interfere with our ability to make, use and sell our products. We do not always conduct independent reviews of pending patent applications of and patents issued to third parties. Patent applications in the United States and elsewhere are typically published approximately 18 months after the earliest filing for which priority is claimed, with such earliest filing date being commonly referred to as the priority date. Certain U.S. applications that will not be filed outside the U.S. can remain confidential until patents issue. In addition, patent applications in the United States and elsewhere can be pending for many years before issuance, or unintentionally abandoned patents or applications can be revived. Furthermore, pending patent applications that have been published can, subject to certain limitations, be later amended in a manner that could cover our technologies, our products or the use of our products. As such, there may be applications of others now pending or recently revived patents of which we are unaware. These patent applications may later result in issued patents, or the revival of previously abandoned patents, that will prevent, limit or otherwise interfere with our ability to make, use or sell our products.

The scope of a patent claim is determined by an interpretation of the law, the written disclosure in a patent and the patent's prosecution history. Our interpretation of the relevance or the scope of a patent or a pending application may be incorrect. For example, we may incorrectly determine that our products are not covered by a third-party patent or may incorrectly predict whether a third-party's pending application will issue with claims of relevant scope. Our determination of the expiration date of any patent in the United States or abroad that we consider relevant may be incorrect. Our failure to identify and correctly interpret relevant patents may negatively impact our ability to develop and market our products.

We cannot provide any assurances that third-party patents do not exist which might be enforced against our current technology, including our research programs, product candidates, their respective methods of use, manufacture and formulations thereof, and could result in either an injunction prohibiting our manufacture or future sales, or, with respect to our future sales, an obligation on our part to pay royalties and/or other forms of compensation to third parties, which could be significant.

If we are sued for infringing intellectual property rights of third parties, such litigation could be costly and time consuming and could prevent or delay us from developing or commercializing our product candidates.

Our commercial success depends, in part, on our ability to develop, manufacture, market and sell our product candidates without infringing the intellectual property and other proprietary rights of third parties. Third parties may allege that we have infringed or misappropriated their intellectual property. Litigation or other legal proceedings relating to intellectual property claims, with or without merit, is unpredictable and generally expensive and time consuming and, even if resolved in our favor, is likely to divert significant resources from our core business, including distracting our 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 market 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 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 have a material adverse effect on our ability to compete in the marketplace.

There is a substantial amount of intellectual property litigation in the biotechnology and pharmaceutical industries, and we may become party to, or threatened with, litigation or other adversarial proceedings regarding intellectual property rights with respect to our products candidates. We cannot be certain that our product candidates and other proprietary technologies we may develop will not infringe existing or future patents owned by third parties. Third parties may assert infringement claims against us based on existing or future intellectual property rights. In the United States, proving invalidity in court requires a showing of clear and convincing evidence to overcome the presumption of validity enjoyed by issued patents. If we are found to infringe a third party's intellectual property rights, we could be forced, including by court order, to cease developing, manufacturing or commercializing the infringing product candidate or product. Alternatively, we may be required to obtain a license from such third party in order to use the infringing technology and continue developing, manufacturing or marketing the infringing product candidate or product. 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 access to the same technologies licensed to us. 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. A finding of infringement could prevent us from commercializing our investigational products or force us to cease some of our business operations, which could materially harm our business.

We may not be aware of patents that have already been issued and that a third party, for example, a competitor in the fields in which we are developing our product candidates, might assert are infringed by our product candidates, including claims to compositions, formulations, methods of manufacture or methods of use or treatment that cover our product candidates. It is also possible that patents owned by third parties of which we are aware, but which we do not believe are relevant to our product candidates and other proprietary technologies we may develop, could be found to be infringed by our product candidate. In addition, because patent applications can take many years to issue, there may be currently pending patent applications that may later result in issued patents that our product candidates may infringe. Our competitors in both the United States and abroad, many of which have substantially greater resources and have made substantial investments in patent portfolios and competing technologies, may have applied for or obtained or may in the future apply for and obtain, patents that will prevent, limit or otherwise interfere with our ability to make, use and sell our product candidates. The pharmaceutical and biotechnology industries have produced a considerable number of patents, and it may not always be clear to industry participants, including us, which patents cover various types of products or methods of use. The coverage of patents is subject to interpretation by the courts, and the interpretation is not always uniform. If we were sued for patent infringement, we would need to demonstrate that our product candidates, products or methods either do not infringe the patent claims of the relevant patent or that the patent claims are invalid or unenforceable, and we may not be able to do this. Proving invalidity may be difficult. For example, in the United States, proving invalidity in court requires a showing of clear and convincing evidence to overcome the presumption of validity enjoyed by issued patents, and there is no assurance that a court of competent jurisdiction would invalidate the claims of any such U.S. patent. Even if we are successful in these proceedings, we may incur substantial costs and the time and attention of our management and scientific personnel could be diverted in pursuing these proceedings, which could have a material adverse effect on our business and operations. 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 litigation. In addition, we may not have sufficient resources to bring these actions to a successful conclusion.

We may choose to challenge the enforceability or validity of claims in a third party's U.S. patent by requesting that the USPTO review the patent claims in an ex-parte re-exam, inter partes review or post-grant review proceedings. These proceedings are expensive and may consume our time or other resources. We may choose to challenge a third party's patent in patent opposition proceedings in the European Patent Office (EPO), or other foreign patent office. The costs of these opposition proceedings could be substantial, and may consume our time or other resources. If we fail to obtain a favorable result at the USPTO, EPO or other patent office then we may be exposed to litigation by a third party alleging that the patent may be infringed by our product candidates or proprietary technologies.

If we are found to infringe a third-party's intellectual property rights, we could be forced, including by court order, to cease developing, manufacturing or commercializing the infringing product candidate or product. Alternatively, we may be required to obtain a license from such third-party in order to use the infringing technology and continue developing, manufacturing or marketing the infringing product candidate. 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 access to the same technologies licensed to us. 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. A finding of infringement could prevent us from commercializing our product candidates or force us to cease some of our business operations, and could divert the time and attention of our technical personnel and management, cause development delays, and/or require us to develop non-infringing technology, which may not be possible on a cost-effective basis, any of which could materially harm our business. In the event of a successful claim of infringement against us, we may have to pay substantial monetary damages, including treble damages and attorneys' fees for willful infringement, pay royalties and other fees, redesign our infringing drug or obtain one or more licenses from third parties, which may be impossible or require substantial time and monetary expenditure. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business.

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

Competitors or other third parties may infringe our patents, trademarks or other intellectual property. To counter infringement or unauthorized use, we may be required to file 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. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe their patents, in addition to counterclaims asserting that our patents are invalid or unenforceable, or both. In patent litigation in the United States, defendant counterclaims alleging invalidity and/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, non-enablement or insufficient written description. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO or made a misleading statement during prosecution. The outcome following legal assertions of invalidity and unenforceability is unpredictable. In any patent infringement proceeding, there is a risk that a court will decide that a patent of ours is invalid or unenforceable, in whole or in part, and that we do not have the right to stop the other party from using the invention at issue. There is also a risk that, even if the validity of such patents is upheld, the court will construe the patent's claims narrowly or decide that we do not have the right to stop the other party from using the invention at issue on the grounds that our patent claims do not cover the invention, or decide that the other party's use of our patented technology falls under the safe harbor to patent infringement under 35 U.S.C. §271(e)(1). An adverse outcome in a litigation or proceeding involving our patents could limit our ability to assert our patents against those parties or other competitors and may curtail or preclude our ability to exclude third parties from making and selling similar or competitive products. Any of these occurrences could adversely affect our competitive business position, business prospects and financial condition. Similarly, if we assert trademark infringement claims, a court may determine that the marks we have asserted are invalid or unenforceable, or that the party against whom we have asserted trademark infringement has superior rights to the marks in question. In this case, we could ultimately be forced to cease use of such trademarks.

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 litigation. There could also 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 material adverse effect on the price of shares of our common stock. Moreover, we cannot assure you that we will have sufficient financial or other resources to file and pursue such infringement claims, which typically last for years before they are concluded. Even if we ultimately prevail in such claims, the monetary cost of such litigation and the diversion of the attention of our management and scientific personnel could outweigh any benefit we receive as a result of the proceedings.

Because of the expense and uncertainty of litigation, we may not be in a position to enforce our intellectual property rights against third parties.

Because of the expense and uncertainty of litigation, we may conclude that even if a third-party is infringing our issued patent, any patents that may be issued as a result of our pending or future patent applications or other intellectual property rights, the risk-adjusted cost of bringing and enforcing such a claim or action may be too high or not in the best interest of our company or our stockholders, or it may be otherwise impractical or undesirable to enforce our intellectual property against some third parties. Our competitors or other third parties may be able to sustain the costs of complex patent litigation or proceedings more effectively than we can because of their greater financial resources and more mature and developed intellectual property portfolios. In such cases, we may decide that the more prudent course of action is to simply monitor the situation or initiate or seek some other non-litigious action or solution. In addition, the uncertainties associated with litigation could compromise our ability to raise the funds necessary to continue our clinical trials, continue our internal research programs, in-license needed technology or other product candidates, or enter into development partnerships that would help us bring our product candidates to market.

We may be subject to claims that we have wrongfully hired an employee from a competitor or that our employees, consultants or independent contractors have wrongfully used or disclosed confidential information of third parties.

As is common in the pharmaceutical industry, in addition to our employees, we engage the services of consultants to assist us in the development of our product candidates. Many of these consultants, and many of our employees, were previously employed at, or may have previously provided or may be currently providing consulting services to, other pharmaceutical companies including our competitors or potential competitors. We could in the future be subject to claims that we or our employees have inadvertently or otherwise used or disclosed alleged trade secrets or other confidential information of former employers or competitors. Although we try to ensure that our employees and consultants do not use the intellectual property, proprietary information, know-how or trade secrets of others in their work for us, we may become subject to claims that we caused an employee to breach the terms of his or her non-competition or non-solicitation agreement, or that we or these individuals have, inadvertently or otherwise, used or disclosed the alleged trade secrets or other proprietary information of a former employer or competitor.

While we may litigate to defend ourselves against these claims, even if we are successful, litigation could result in substantial costs and could be a distraction to management. If our defenses to these claims fail, in addition to requiring us to pay monetary damages, a court could prohibit us from using technologies or features that are essential to our product candidates, if such technologies or features are found to incorporate or be derived from the trade secrets or other proprietary information of the former employers. Moreover, any such litigation or the threat thereof may adversely affect our reputation, our ability to form strategic alliances or sublicense our rights to collaborators, engage with scientific advisors or hire employees or consultants, each of which would have an adverse effect on our business, results of operations and financial condition. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.

We may rely on trade secrets and proprietary know-how which can be difficult to trace and enforce and, if we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

In addition to seeking patents for some of our technology and product candidates, we may also rely on trade secrets, including unpatented know-how, technology and other proprietary information, to maintain our competitive position. Elements of our product candidate, including processes for their preparation and manufacture, may involve proprietary know-how, information, or technology that is not covered by patents, and thus for these aspects we may consider trade secrets and know-how to be our primary intellectual property. Any disclosure, either intentional or unintentional, by our employees, the employees of third parties with whom we share our facilities or third-party consultants and vendors that we engage to perform research, clinical trials or manufacturing activities, or misappropriation by third parties (such as through a security incident) of our trade secrets or proprietary information could enable competitors to duplicate or surpass our technological achievements, thus eroding our competitive position in our market. Because we expect to rely on third parties in the development and manufacture of our product candidates, we must, at times, share trade secrets with them. Our reliance on third parties requires us to share our trade secrets, which increases the possibility that a competitor will discover them or that our trade secrets will be misappropriated or disclosed.

Trade secrets and know-how can be difficult to protect. We require our employees to enter into written employment agreements containing provisions of confidentiality and obligations to assign to us any inventions generated in the course of their employment. We and any third parties with whom we share facilities enter into written agreements that include confidentiality and intellectual property obligations to protect each party's property, potential trade secrets, proprietary know-how, and information. We further seek to protect our potential trade secrets, proprietary know-how, and information in part, by entering into non-disclosure and confidentiality agreements with parties who are given access to them, such as our corporate collaborators, outside scientific collaborators, contract research organizations, contract manufacturers, consultants, advisors and other third parties. With our consultants, contractors, and outside scientific collaborators, these agreements typically include invention assignment obligations. 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 cannot be certain that our trade secrets and other confidential proprietary information will not be disclosed or that competitors will not otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques. Despite these efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. 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. If any of our trade secrets were to be disclosed to or independently developed by a competitor or other third-party, our competitive position would be harmed.

We may become subject to claims challenging the inventorship or ownership of our patents and other intellectual property.

We may be subject to claims that former employees, collaborators or other third parties have an interest in our patents or other intellectual property as an inventor or co-inventor. The failure to name the proper inventors on a patent application can result in the patents issuing thereon being unenforceable. Inventorship disputes may arise from conflicting views regarding the contributions of different individuals named as inventors, the effects of foreign laws where foreign nationals are involved in the development of the subject matter of the patent, conflicting obligations of third parties involved in developing our product candidates or as a result of questions regarding co-ownership of potential joint inventions. Litigation may be necessary to resolve these and other claims challenging inventorship and/or ownership. Alternatively, or additionally, we may enter into agreements to clarify the scope of our rights in such intellectual property. If we 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, valuable intellectual property. Such an outcome could have a material adverse effect on our business. 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.

Our licensors may have relied on third-party consultants or collaborators or on funds from third parties, such as the U.S. government, such that our licensors are not the sole and exclusive owners of the patents we in-licensed. If other third parties have ownership rights or other rights to our in-licensed patents, they may be able to license such patents to our competitors, and our competitors could market competing products and technology. This could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects.

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. 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. Such claims could have a material adverse effect on our business, financial condition, results of operations, and prospects.

Patent terms may be inadequate to protect our competitive position on our product candidates for an adequate amount of time.

Patent rights are of limited duration. In the United States, if all maintenance fees are paid timely, the natural expiration of a patent is generally 20 years after its first effective filing date. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such product candidates are commercialized. Even if patents covering our product candidates are obtained, once the patent life has expired for a product, we may be open to competition from biosimilar or generic products. As a result, our patent portfolio may not provide us with sufficient rights to exclude others from commercializing product candidates similar or identical to ours. Upon issuance in the United States, the term of a patent can be increased by patent term adjustment, which is based on certain delays caused by the USPTO, but this increase can be reduced or eliminated based on certain delays caused by the patent applicant during patent prosecution. The term of a United States patent may also be shortened if the patent is terminally disclaimed over an earlier-filed patent. A patent term extension (PTE) based on regulatory delay may be available in the United States. However, only a single patent can be extended for each marketing approval, and any patent can be extended only once, for a single product. Moreover, the scope of protection during the period of the PTE does not extend to the full scope of the claim, but instead only to the scope of the product as approved. Laws governing analogous PTEs in foreign jurisdictions vary widely, as do laws governing the ability to obtain multiple patents from a single patent family. Additionally, we may not receive an extension if we fail to exercise due diligence during the testing phase or regulatory review process, apply within applicable deadlines, fail to apply prior to expiration of relevant patents or otherwise fail to satisfy applicable requirements. If we are unable to obtain PTE or restoration, or the term of any such extension is less than we request, the period during which we will have the right to exclusively market our product will be shortened and our competitors may obtain approval of competing products following our patent expiration and may take advantage of our investment in development and clinical trials by referencing our clinical and preclinical data to launch their product earlier than might otherwise be the case, and our revenue could be reduced, possibly materially.

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 or future trademarks or trade names may be challenged, infringed, circumvented or declared generic or descriptive or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names or may be forced to stop using these names, which we need for name recognition by potential partners or customers in our markets of interest. During trademark registration proceedings, we may receive rejections of our applications by the USPTO or in other foreign jurisdictions. Although we would be given an opportunity to respond to those rejections, we may be unable to overcome such rejections. In addition, in the USPTO and in comparable agencies in many foreign jurisdictions, third parties are given an opportunity to oppose pending trademark applications and to seek to cancel registered trademarks. Opposition or cancellation proceedings may be filed against our trademarks, and our trademarks may not survive such proceedings. If we are unable to establish name recognition based on our trademarks and trade names, we may not be able to compete effectively and our business may be adversely affected. We may license our trademarks and trade names to third parties, such as distributors. Although these license agreements may provide guidelines for how our trademarks and trade names may be used, a breach of these agreements or misuse of our trademarks and tradenames by our licensees may jeopardize our rights in or diminish the goodwill associated with our trademarks and trade names.

Moreover, any name we have proposed to use with our product candidate in the United States must be approved by the FDA, regardless of whether we have registered it, or applied to register it, as a trademark. Similar requirements exist in Europe. The FDA typically conducts a review of proposed product names, including an evaluation of potential for confusion with other product names. If the FDA (or an equivalent administrative body in a foreign jurisdiction) objects to any of our proposed proprietary product names, it may be required to expend significant additional resources in an effort to identify a suitable substitute name that would qualify under applicable trademark laws, not infringe the existing rights of third parties and be acceptable to the FDA. Furthermore, in many countries, owning and maintaining a trademark registration may not provide an adequate defense against a subsequent infringement claim asserted by the owner of a senior trademark. At times, competitors or other 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. If we assert trademark infringement claims, a court may determine that the marks we have asserted are invalid or unenforceable, or that the party against whom we have asserted trademark infringement has superior rights to the marks in question. In this case, we could ultimately be forced to cease use of such trademarks.

Risks Related to the Securities Market and Ownership of Our Common Stock

An active trading market for our common stock may not be sustained, which may make it difficult for you to sell your shares.

Prior to our initial public offering in March 2021, there had been no public market for our common stock. The trading market for our common stock on The Nasdaq Global Select Market has been limited and an active trading market for our shares may not be sustained. If an active market for our common stock is not sustained, it may be difficult for you to sell your shares at a price that is attractive to you, or at all.

The price of our common stock could be subject to volatility related or unrelated to our operations.

Our stock price may be volatile. The stock market in general and the market for biotechnology and pharmaceutical companies, in particular, have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, you may not be able to sell your shares at a price that is attractive to you, or at all. The market price for our common stock may be influenced by numerous factors, many of which are beyond our control, including:

- overall performance of the equity markets;
- our operating performance and the performance of other similar companies;
- the published opinions and third-party valuations by banking and market analysts;
- results from our ongoing clinical trials and future clinical trials with our current and future product candidates or of our competitors;
- adverse results or delays in preclinical studies;
- failure to commercialize our product candidates;
- unanticipated serious safety concerns related to the use of our product candidates;
- changes in our projected operating results that we provide to the public, our failure to meet these projections or changes in recommendations by securities analysts that elect to follow our common stock;
- any delay in our regulatory filings for our product candidates and any adverse development or perceived adverse development with respect to the applicable regulatory authority's review of such filings, including without limitation the FDA's issuance of a "refusal to file" letter or a request for additional information;

- regulatory or legal developments in the United States and other countries;
- changes in the structure of healthcare payment systems;
- the level of expenses related to our product candidates or clinical development programs;
- our failure to achieve product development goals in the timeframe we announce;
- announcements of acquisitions, strategic alliances or significant agreements by us or by our competitors;
- recruitment or departure of key personnel;
- the economy as a whole and market conditions in our industry;
- trading activity by our principal stockholders;
- the size of our market float;
- political uncertainty and/or instability in the United States;
- wars, military conflicts and other geopolitical events;
- global supply chain and/or labor shortage challenges;
- a resurgence of COVID-19 or other health epidemic or pandemic and actions taken to slow its spread; and
- any other factors discussed in this report.

In addition, the stock markets have experienced extreme price and volume fluctuations that have affected and continue to affect the market prices of equity securities of many biopharmaceutical companies. Stock prices of many biopharmaceutical companies have fluctuated in a manner unrelated or disproportionate to the operating performance of those companies. The trading prices for common stock of other biopharmaceutical companies have also been highly volatile recently. In the past, stockholders have filed securities class action litigation following periods of market volatility. If we were to become involved in securities litigation, it could subject us to substantial costs, divert resources and the attention of management from our business and adversely affect our business.

Our principal stockholders and management own a significant percentage of our stock and will be able to exert significant control over matters subject to stockholder approval.

Certain of our executive officers, directors and large stockholders own a significant percentage of our outstanding capital stock. As a result of their share ownership, these stockholders will have the ability to influence us through their ownership positions. These stockholders may be able to determine all matters requiring stockholder approval. For example, these stockholders, acting together, may be able to control elections of directors, amendments of our organizational documents, or approval of any merger, sale of assets, or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for our common stock that you may believe are in your best interest as one of our stockholders.

Future sales and issuances of our common stock or rights to purchase common stock, including pursuant to our equity incentive plans, could result in additional dilution of the percentage ownership of our stockholders and could cause our stock price to fall.

Additional capital will be needed in the future to continue our planned operations. To the extent we raise additional capital by issuing equity securities, our stockholders may experience substantial dilution. We may sell common stock, convertible securities or other equity securities in one or more transactions at prices and in a manner, we determine from time to time. If we sell common stock, convertible securities or other equity securities in more than one transaction, investors may be materially diluted by subsequent sales. These sales may also result in material dilution to our existing stockholders, and new investors could gain rights superior to our existing stockholders.

Pursuant to our 2021 Plan, our management is authorized to grant stock options and other equity-based awards to our employees, directors and consultants. The number of shares of our common stock reserved for issuance under our 2021 Plan will automatically increase on January 1 of each calendar year, starting on January 1, 2022 through January 1, 2031, in an amount equal to the lesser of (i) 5% of the total number of shares of our common stock outstanding on the last day of the calendar month before the date of each automatic increase; or (ii) a lesser number of shares determined by our board of directors prior to the applicable January 1st. In addition, our 2021 Employee Stock Purchase Plan (ESPP) authorizes the issuance of 600,000 shares of our common stock under purchase rights granted to our employees or to employees of any of our designated affiliates. The number of shares of our common stock reserved for issuance under the ESPP will automatically increase on January 1 of each calendar year by the lesser of 1% of the total number of shares of our common stock outstanding on December 31 of the preceding calendar year and 1,200,000 shares, subject to the ability of our Board of Directors to take action to reduce the size of the increase in any given year. Increases in the number of shares available for future grant or purchase may result in additional dilution, which could cause our stock price to fall.

We do not intend to pay dividends on our common stock so any returns will be limited to the value of our stock.

We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. Any return to stockholders will therefore be limited to the appreciation of their stock.

We are an “emerging growth company”, and we intend to take advantage of reduced reporting requirements.

We are an “emerging growth company” as defined in the JOBS Act, and we intend to take advantage of some of the exemptions from reporting requirements that are applicable to other public companies that are not emerging growth companies, including:

- 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
- not being required to hold a non-binding advisory vote on executive compensation or obtain stockholder approval of any golden parachute payments not previously approved.

We may take advantage of these reporting exemptions until we are no longer an emerging growth company. We will remain an emerging growth company until the earlier of (i) December 31, 2026 (the last day of the fiscal year following the fifth anniversary of the completion of our initial public offering), (ii) the last day of the fiscal year in which we have total annual gross revenue of at least \$1.235 billion, (iii) the date upon which we are deemed to be a “large accelerated filer”, which means we have been subject to the reporting requirements of the Securities Exchange Act of 1934, as amended (Exchange Act), for at least 12 months as of December 31st, and the market value of our common stock that is held by non-affiliates exceeds \$700 million as of the prior June 30th and (iv) the date on which we have issued more than \$1.0 billion in non-convertible debt during the prior three-year period.

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

As a public company listed on the Nasdaq Global Select Market, we incur significant expenses for director and officer insurance, legal services, accounting services and other expenses that we did not incur as a private company. In addition, the Sarbanes-Oxley Act, as well as rules subsequently implemented by the SEC, and the Nasdaq Global Select Market have imposed various requirements on public companies. In July 2010, the Dodd-Frank Wall Street Reform and Consumer Protection Act (the Dodd-Frank Act) was enacted. There are significant corporate governance and executive compensation related provisions in the Dodd-Frank Act that required the SEC to adopt rules and regulations in these areas such as “say on pay” and proxy access. Recent legislation permits smaller “emerging growth companies” to implement many of these requirements over a longer period and up to five years from the pricing of our initial public offering. We intend to continue to take advantage of this legislation but cannot guarantee that we will not be required to implement these requirements sooner than budgeted or planned and thereby incur unexpected expenses. Stockholder activism, the current political environment and the current high level of government intervention and regulatory reform may lead to substantial new regulations and disclosure obligations, which may lead to additional compliance costs and impact the manner in which we operate our business in ways we cannot currently anticipate. Our management and other personnel will need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations increase our legal and financial compliance costs and make some activities more time-consuming and costlier. For example, these rules and regulations make it more difficult and more expensive for us to obtain director and officer liability insurance and we are required to incur substantial costs to maintain our current levels of such coverage.

If we fail to maintain an effective system of disclosure controls and internal control over financial reporting, our ability to produce timely and accurate financial statements or comply with applicable regulations could be impaired.

As a public company, we are subject to requirements of the Sarbanes-Oxley Act, the regulations of the Nasdaq Global Select Market, the rules and regulations of the SEC, expanded disclosure requirements, accelerated reporting requirements and more complex accounting rules. We expect that the requirements of these rules and regulations will continue to increase our legal, accounting and financial compliance costs, make some activities more difficult, time-consuming and costly and place significant strain on our personnel, systems and resources. Company responsibilities required by the Sarbanes-Oxley Act include, among other things, that we maintain corporate oversight and adequate internal control over financial reporting and disclosure controls and procedures. We are continuing to develop and refine our disclosure controls and other procedures that are designed to ensure that information required to be disclosed by us in the reports that we file with the SEC is recorded, processed, summarized and reported within the time periods specified in SEC rules and forms and that information required to be disclosed in reports under the Exchange Act is accumulated and communicated to our principal executive and financial officers. We are also continuing to improve our internal control over financial reporting. In order to develop, maintain, and improve the effectiveness of our internal controls and procedures, and internal control over financial reporting, we have expended, and anticipate that we will continue to expend, significant resources, including accounting-related costs and significant management oversight.

Our current controls and any new controls that we develop may become inadequate because of changes in conditions in our business. Further, weaknesses in our disclosure controls and internal control over financial reporting may be discovered in the future. Any failure to develop or maintain effective controls or any difficulties encountered in their implementation or improvement could harm our results of operations or cause us to fail to meet our reporting obligations and may result in a restatement of our financial statements for prior periods. Any failure to implement and maintain effective internal control over financial reporting could also adversely affect the results of periodic management evaluations and annual independent registered public accounting firm attestation reports regarding the effectiveness of our internal control over financial reporting that we will eventually be required to include in our periodic reports that will be filed with the SEC. Ineffective disclosure controls and procedures and internal control over financial reporting could also cause investors to lose confidence in our reported financial and other information, which would likely have a negative effect on the trading price of our common stock. In addition, if we are unable to continue to meet these requirements, we may not be able to remain listed on the Nasdaq Global Select Market.

If we cannot provide reliable financial reports or prevent fraud, our business and results of operations could be harmed, investors could lose confidence in our reported financial information and we could be subject to sanctions or investigations by Nasdaq, the SEC or other regulatory authorities. Any failure to maintain effective disclosure controls and internal control over financial reporting could have a material and adverse effect on our business, results of operations and financial condition and could cause a decline in the trading price of our common stock.

Future changes in financial accounting standards or practices may cause adverse and unexpected revenue fluctuations and adversely affect our reported results of operations.

Future changes in financial accounting standards may cause adverse, unexpected revenue fluctuations and affect our reported financial position or results of operations. Financial accounting standards in the United States are constantly under review and new pronouncements and varying interpretations of pronouncements have occurred with frequency in the past and are expected to occur again in the future. As a result, we may be required to make changes in our accounting policies. Those changes could affect our financial condition and results of operations or the way in which such financial condition and results of operations are reported. We intend to invest resources to comply with evolving standards, and this investment may result in increased general and administrative expenses and a diversion of management time and attention from business activities to compliance activities. See the section titled “Management’s Discussion and Analysis of Financial Condition and Results of Operations—Recent Accounting Pronouncements.

Changes in tax laws or regulations that are applied adversely to us or our customers may have a material adverse effect on our business, cash flow, financial condition or results of operations.

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 operations and financial performance. Further, existing tax laws, statutes, rules, regulations or ordinances could be interpreted, changed, modified or applied adversely to us. For example, legislation informally titled the Tax Cuts and Jobs Act; the Coronavirus Aid, Relief, and Economic Security Act; and the Inflation Reduction Act enacted many significant changes to the U.S. tax laws. Future guidance from the Internal Revenue Service and other tax authorities with respect to such legislation may affect us, and certain aspects of such legislation could be repealed or modified in future legislation. The Biden administration and Congress could also enact other tax law changes that could have an adverse effect on our operations, cash flows and results from operations and contribute to overall market volatility. In addition, it is uncertain if and to what extent various states will conform to federal tax legislation. Changes in corporate tax rates, the realization of net deferred tax assets relating to our operations, the taxation of foreign earnings, and the deductibility of expenses could have a material impact on the value of our deferred tax assets, could result in significant one-time charges, and could increase our future U.S. tax expense.

Our information technology systems or sensitive data, or those of our third-party CROs or other contractors or consultants, may fail or suffer security incidents, loss or leakage of data, and other disruptions, which could result in a material disruption of our product candidates’ development programs, compromise sensitive data related to our business or prevent us from accessing critical information, potentially exposing us to liability or otherwise adversely affecting our business.

We are increasingly dependent upon information technology systems, infrastructure and data to operate our business. In the ordinary course of business, we or our third-party CROs or other contractors or consultants acting on our behalf may collect, receive, store, process, generate, use, transfer, disclose, make accessible, protect, secure, dispose of, transmit, and share (collectively, processing) proprietary, confidential, and sensitive data (including but not limited to intellectual property, proprietary business information, health-related data, and personal data). We also have outsourced elements of our operations to third parties, and as a result we rely on a number of third-party contractors who have access to our proprietary, confidential, and sensitive data. We share or receive sensitive data with or from third parties. Our ability to monitor these third parties’ cybersecurity practices is limited, and these third parties may not have adequate information security measures in place.

Cyberattacks, malicious internet-based activity, and online and offline fraud are prevalent and continue to increase. These threats are becoming increasingly difficult to detect. These threats come from a variety of sources, including traditional computer “hackers,” threat actors, personnel misconduct or error (such as theft or misuse), sophisticated nation-state and nation-state supported actors. Some actors now engage and are expected to continue to engage in cyber-attacks, including, without limitation, nation-state actors for geopolitical reasons and in conjunction with military conflicts and defense activities. During times of war and other major conflicts, we and the third parties upon which we rely may be vulnerable to a heightened risk of these attacks, including cyber-attacks, that could materially disrupt our systems and operations, supply chain, and ability to produce, sell and distribute our goods and services. We and our third-party CROs or other contractors or consultants, may be subject to a variety of evolving threats, including but not limited to social engineering attacks (including through phishing attacks), malicious code (such as viruses and worms), malware (including as a result of advanced persistent threat intrusions), denial-of-service attacks (such as credential stuffing), ransomware attacks, supply-chain attacks, software bugs, server malfunction, software or hardware failures, loss of data or other information technology assets, adware, telecommunications failures, earthquakes, fire, flood, and other similar threats. Ransomware attacks, including those perpetrated by organized criminal threat actors, nation-states, and nation-state supported actors, are becoming increasingly prevalent and severe and can lead to significant interruptions in our operations, loss of data and income, reputational harm, and diversion of funds. Extortion payments may alleviate the negative impact of a ransomware attack, but we may be unwilling or unable to make such payments due to, for example, applicable laws or regulations prohibiting payments. Similarly, supply-chain attacks have increased in frequency and severity, and we cannot guarantee that third parties and infrastructure in our supply chain have not been compromised or that they do not contain exploitable defects or bugs that could result in a breach of or disruption to our information technology systems or the third-party information technology systems that support us and our services. Remote work has become more common and has increased risks to our information technology systems and data, as more of our employees utilize network connections, computers and devices outside our premises or network, including working at home, while in transit and in public locations.

Any of the previously identified or similar threats could cause a security incident or other interruption. A security incident or other interruption could result in unauthorized, unlawful or accidental acquisition, modification, destruction, loss, alteration, encryption, disclosure of or access to data. A security incident or other interruption could disrupt our (and third parties upon whom we rely) ability to develop or provide our products. We may expend significant resources or modify our business activities (including our clinical trial activities) in an effort to protect against security incidents. Additionally, certain data privacy and security obligations may require us to implement and maintain specific security measures, industry-standard or reasonable security measures to protect our information technology systems and data.

While we have implemented measures designed to protect against security incidents, our security measures may in the future not be sufficient to prevent security incidents. We have no control over the security measures of third parties with whom we share or receive sensitive data. We take steps to detect and remediate vulnerabilities, but we may not be able to detect and remediate all vulnerabilities because the threats and techniques used to exploit the vulnerability change frequently and are often sophisticated in nature. Therefore, such vulnerabilities could be exploited but may not be detected until after a security incident has occurred. These vulnerabilities pose material risks to our business. Further, we may experience, delays in developing and deploying remedial measures designed to address any such identified vulnerabilities.

Applicable data privacy and security obligations may require us to notify relevant stakeholders of security incidents. Such disclosures are costly, and the disclosures or the failure to comply with such requirements, could lead to adverse impacts. If we (or a third party upon whom we rely) experience a security incident or are perceived to have experienced a security incident, we may experience adverse consequences. These consequences may include the following: government enforcement actions (for example, investigations, fines, penalties, audits, and inspections); additional reporting requirements and/or oversight; restrictions on processing data (including personal data); litigation (including class claims); indemnification obligations; negative publicity; reputational harm; monetary fund diversions; interruptions in our operations (including availability of data); financial loss; and other similar harms. Security incidents and attendant consequences may cause customers to stop using our products, deter new customers for using our products, and negatively impact our ability to grow and operate our business.

Our contracts may not contain limitations of liability, and even where they do, there can be no assurance that limitations of liability in our contracts are sufficient to protect us from liabilities, damages, or claims related to our data privacy and security obligations. We cannot be sure that our insurance coverage will be adequate or sufficient to protect us from or to mitigate liabilities arising out of our privacy and security practices, that such coverage will continue to be available on commercially reasonable terms or at all, or that such coverage will pay future claims.

We or the third parties upon whom we depend may be adversely affected by earthquakes, fires or other natural disasters and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.

Our corporate headquarters and research facility are located in the county of San Diego, California, which in the past has experienced severe earthquakes and fires. If these earthquakes, fires, other natural disasters, terrorism and similar unforeseen events beyond our control prevented us from using all or a significant portion of our headquarters or research facility, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. We do not have a disaster recovery or business continuity plan in place and may incur substantial expenses as a result of the absence or limited nature of our internal or third-party service provider disaster recovery and business continuity plans, which, particularly when taken together with our lack of earthquake insurance, could have a material adverse effect on our business. Furthermore, integral parties in our supply chain are operating from single sites, increasing their vulnerability to natural disasters or other sudden, unforeseen and severe adverse events. If such an event were to affect our supply chain, it could have a material adverse effect on our ability to conduct our clinical trials, our development plans and business.

We are subject to certain U.S. and foreign anti-corruption, anti-money laundering, export control, sanctions, and other trade laws and regulations. We can face serious consequences for violations.

U.S. and foreign anti-corruption, anti-money laundering, export control, sanctions, and other trade laws and regulations (collectively, Trade Laws), prohibit, among other things, companies and their employees, agents, CROs, legal counsel, accountants, consultants, contractors, and other partners from authorizing, promising, offering, providing, soliciting, or receiving directly or indirectly, corrupt or improper payments or anything else of value to or from recipients in the public or private sector. Violations of Trade Laws can result in substantial criminal fines and civil penalties, imprisonment, the loss of trade privileges, debarment, tax reassessments, breach of contract and fraud litigation, reputational harm, and other consequences. We have direct or indirect interactions with officials and employees of government agencies or government-affiliated hospitals, universities, and other organizations. We also expect our non-U.S. activities to increase over time. We expect to rely on third parties for research, preclinical studies, and clinical trials and/or to obtain necessary permits, licenses, patent registrations, and other marketing approvals. We can be held liable for the corrupt or other illegal activities of our personnel, agents, or partners, even if we do not explicitly authorize or have prior knowledge of such activities.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business.

We, and the third parties with whom we share our facilities, are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological and radioactive materials. Our operations also produce hazardous waste products. 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. We could be held liable for any resulting damages in the event of contamination or injury resulting from the use of hazardous materials by us or the third parties with whom we share our facilities or contract with, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties.

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 maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research and development. Failure to comply with these laws and regulations may also result in substantial fines, penalties or other sanctions.

Delaware law and provisions in our amended and restated certificate of incorporation and amended and restated bylaws could make a merger, tender offer or proxy contest difficult, thereby depressing the trading price of our common stock.

Our status as a Delaware corporation and the anti-takeover provisions of the Delaware General Corporation Law (DGCL) may discourage, delay or prevent a change in control by prohibiting us from engaging in a business combination with an interested stockholder for a period of three years after the person becomes an interested stockholder, even if a change of control would be beneficial to our existing stockholders. In addition, our amended and restated certificate of incorporation and amended and restated bylaws contain provisions that may make the acquisition of our company more difficult, including the following:

- a classified board of directors with three-year staggered terms, which could delay the ability of stockholders to change the membership of a majority of our board of directors;
- the ability of our board of directors to issue shares of preferred stock and to determine the price and other terms of those shares, including preferences and voting rights, without stockholder approval, which could be used to significantly dilute the ownership of a hostile acquirer;
- the exclusive right of our board of directors to elect a director to fill a vacancy created by the expansion of our board of directors or the resignation, death or removal of a director, which prevents stockholders from being able to fill vacancies on our board of directors;
- a prohibition on stockholder action by written consent, which forces stockholder action to be taken at an annual or special meeting of our stockholders;
- the requirement that a special meeting of stockholders may be called only by a majority vote of our entire board of directors, the chairman of our board of directors or our chief executive officer, which could delay the ability of our stockholders to force consideration of a proposal or to take action, including the removal of directors;
- the requirement for the affirmative vote of holders of at least 66 2/3% of the voting power of all of the then-outstanding shares of the voting stock, voting together as a single class, to amend the provisions of our amended and restated certificate of incorporation relating to the management of our business or our amended and restated bylaws, which may inhibit the ability of an acquirer to affect such amendments to facilitate an unsolicited takeover attempt; and
- advance notice procedures with which stockholders must comply to nominate candidates to our board of directors or to propose matters to be acted upon at a stockholders' meeting, which may discourage or deter a potential acquirer from conducting a solicitation of proxies to elect the acquirer's own slate of directors or otherwise attempting to obtain control of us.

In addition, as a Delaware corporation, we are subject to Section 203 of the DGCL. These provisions may prohibit large stockholders, in particular those owning 15% or more of our outstanding voting stock, from merging or combining with us for a certain period of time. A Delaware corporation may opt out of this provision by express provision in its original certificate of incorporation or by amendment to its certificate of incorporation or bylaws approved by its stockholders. However, we have not opted out of this provision.

These and other provisions in our amended and restated certificate of incorporation, amended and restated bylaws and Delaware law could make it more difficult for stockholders or potential acquirors to obtain control of our board of directors or initiate actions that are opposed by our then-current board of directors, including delay or impede a merger, tender offer or proxy contest involving our company.

The existence of these provisions could negatively affect the price of our common stock and limit opportunities for you to realize value in a corporate transaction.

Our amended and restated certificate of incorporation provides that the Court of Chancery of the State of Delaware and the federal district courts of the United States of America will be the exclusive forums for substantially all disputes between us and our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Our amended and restated certificate of incorporation provides that the Court of Chancery of the State of Delaware is the exclusive forum for the following types of actions or proceedings under Delaware statutory or common law: (i) any derivative action or proceeding brought on our behalf; (ii) any action asserting a claim of breach of a fiduciary duty; (iii) any action or proceeding asserting a claim against us or any of our current or former directors, officers or other employees, arising out of or pursuant to any provision of the DGCL, our amended and restated certificate of incorporation or our amended and restated bylaws; and (iv) any action asserting a claim against us or any of our directors, officers or other employees, governed by the internal affairs doctrine; provided, that, this provision would not apply to suits brought to enforce a duty or liability created by the Exchange Act, or any other claim for which the federal courts have exclusive jurisdiction.

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 certificate of incorporation further provides that the federal district courts of the United States of America will be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act.

These exclusive-forum provisions may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees and may discourage these types of lawsuits against us and our directors, officers, and other employees. While the Delaware courts have determined that such choice of forum provisions are facially valid, and several state trial courts have enforced such provisions and required that suits asserting Securities Act claims be filed in federal court, there is no guarantee that courts of appeal will affirm the enforceability of such provisions and 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 certificate of incorporation. 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. If a court were to find either exclusive forum provision in our amended and restated certificate of incorporation to be inapplicable or unenforceable in an action, we may incur further significant additional costs associated with litigating Securities Act claims in state court, both state and federal court, or other jurisdictions which could seriously harm our business, financial condition, results of operations, and prospects.

We could be subject to securities class action litigation.

In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because pharmaceutical companies have experienced significant stock price volatility in recent years. If we face such litigation, it could result in substantial costs and a diversion of management's attention and resources, which could harm our business.

General Risk Factors

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

The global credit and financial markets have experienced extreme volatility and disruptions in the past. These disruptions have resulted or can result in severely diminished liquidity and credit availability, high inflation, rising interest rates, declines in consumer confidence, declines in economic growth, increases in unemployment rates and uncertainty about economic stability. There can be no assurance that further deterioration in credit and financial markets and confidence in economic conditions will not occur. Our general business strategy may be adversely affected by any such economic downturn, volatile business environment, higher inflation, or continued unpredictable and unstable market conditions. If the current equity and credit markets deteriorate, it may make any necessary debt or equity financing more difficult, more costly and more dilutive. Our portfolio of investment securities could also be adversely impacted. Failure to secure any necessary financing in a timely manner and on favorable terms could have a material adverse effect on our operations, growth strategy, financial performance and stock price and could require us to delay or abandon clinical or research development plans. In addition, there is a risk that one or more of our current service providers, manufacturers and other partners may not survive an economic downturn or rising inflation, which could directly affect our ability to attain our operating goals on schedule and on budget.

Other international and geo-political events could also have a serious adverse impact on our business. For instance, in February 2022, Russia initiated military action against Ukraine. In response, the United States and certain other countries imposed significant sanctions and trade actions against Russia and could impose further sanctions, trade restrictions, and other retaliatory actions. While we cannot predict the broader consequences, the conflict and retaliatory and counter-retaliatory actions has affected and could further affect, potentially materially and adversely, global trade, currency exchange rates, inflation, regional economies, and the global economy, which in turn may increase our costs, disrupt our supply chain, impair our ability to raise or access additional capital when needed on acceptable terms, if at all, or otherwise adversely affect our business, financial condition, and results of operations.

If there are substantial sales of shares of our common stock, the market price of our common stock could decline.

The price of our common stock could decline if there are substantial sales of our common stock, particularly sales by our directors, executive officers and significant stockholders, or if there is a large number of shares of our common stock available for sale and the market perceives that sales will occur.

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

We are subject to the periodic reporting requirements of the Exchange Act. We designed our disclosure controls and procedures to reasonably assure that information we must disclose in reports we file or submit under the Exchange Act is accumulated and communicated to management, and 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. For example, our directors or executive officers could inadvertently fail to disclose a new relationship or arrangement causing us to fail to make any related party transaction disclosures. 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 due to error or fraud may occur and not be detected.

If securities or industry analysts publish inaccurate or unfavorable research about our business, our stock price and trading volume could decline.

The trading market for our common stock will depend in part on the research and reports that securities or industry analysts publish about us or our business. If only very few securities analysts commence coverage of us, or if industry analysts cease coverage of us, the trading price for our common stock would be negatively affected. If one or more of the analysts who cover us downgrade our common stock or publish inaccurate or unfavorable research about our business, our common stock price would likely decline. If one or more of these analysts cease coverage of us or fail to publish reports on us regularly, demand for our common stock could decrease, which might cause our common stock price and trading volume to decline.

Item 1B. Unresolved Staff Comments.

None.

Item 2. Properties.

We lease approximately 12,370 square feet of laboratory and office space in Carlsbad, California, pursuant to a lease agreement, with a related party, that commenced in September 2021 and expires in August 2027. Additionally, we lease approximately 4,900 square feet of additional office space in the same building, pursuant to a lease amendment, with a related party, that commenced in June 2022 and expires in August 2027. We believe that these facilities will meet our current and near term needs and that suitable additional space will be available as and when needed.

Item 3. Legal Proceedings.

From time to time, we may be involved in legal proceedings arising in the ordinary course of our business. We are not presently a party to any legal proceedings that, in the opinion of management, would have a material adverse effect on our business. Regardless of outcome, litigation can have an adverse impact on us due to defense and settlement costs, diversion of management resources, negative publicity and reputation harm, and other factors.

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 been listed on the Nasdaq Global Market under the symbol “DSGN” since March 25, 2021. Prior to that date, there was no public market for our common stock.

Holders of Common Stock

As of March 9, 2023, there were 55,943,314 shares of common stock issued and held by approximately 15 stockholders of record. The actual number of stockholders is greater than this number of record holders and includes stockholders who are beneficial owners but whose shares are held in street name by brokers and other nominees.

Dividend Policy

We have never declared or paid any cash dividends on our capital stock. We currently intend to retain all available funds and any future earnings to support our operations and finance the growth and development of our business. We do not intend to pay cash dividends on our common stock for the foreseeable future. Any future determination related to our dividend policy will be made at the discretion of our board of directors and will depend upon, among other factors, our results of operations, financial condition, capital requirements, contractual restrictions, business prospects and other factors our board of directors may deem relevant.

Use of Proceeds

On March 25, 2021, we commenced our initial public offering pursuant to a registration statement on Form S-1 (File No. 333-253954) that was declared effective by the SEC on March 25, 2021, for 12,000,000 shares of our common stock for sale to the public at a price of \$20.00 per share. In addition, in March 2021, the underwriters exercised their over-allotment option to purchase 1,800,000 additional shares of our common stock in the initial public offering at the public offering price of \$20.00 per share, such that the aggregate offering price of our initial public offering was \$276.0 million. The net offering proceeds to us, after deducting underwriting discounts and commissions and offering costs, were \$254.3 million. No offering expenses were paid directly or indirectly to any of our directors or officers (or their associates) or persons owning 10% or more of any class of our equity securities or to any other affiliates. The underwriters for our initial public offering were Goldman Sachs & Co. LLC, SVB Leerink LLC, and Piper Sandler & Co.

The net proceeds from our initial public offering are being held in cash, cash equivalents and investments securities, primarily in money market funds invested in U.S. government agency securities and U.S. treasury securities. These investments are made pursuant to our investment policy and we may further invest these funds in high-quality marketable debt instruments of corporations and government sponsored enterprises with contractual maturity dates of generally less than two years until needed to fund our operations. There has been no material change in the use of proceeds from our initial public offering as described in our final prospectus filed with the SEC pursuant to Rule 424(b)(4) on March 26, 2021. As of December 31, 2022, we had used approximately \$50.0 million of the net proceeds received from our initial public offering to support our operations.

Issuer Purchases of Equity Securities

None.

Sale of Unregistered Securities

None.

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 notes thereto included in "Item 8. Financial Statements and Supplementary Data" of this Annual Report on Form 10-K. In addition to historical information, this Annual Report contains forward-looking statements that involve risks, uncertainties, and assumptions. Our actual results may differ materially from those anticipated in these forward-looking statements as a result of certain factors, including but not limited to those set forth under the caption "Item 1A. Risk Factors."

Overview

We are a clinical-stage biopharmaceutical company pioneering the research and development of GeneTAC™ molecules, which are a novel class of small-molecule gene targeted chimera therapeutic candidates designed to be disease-modifying by addressing the underlying cause of diseases caused by inherited nucleotide repeat expansion mutations. Certain diseases caused by inherited nucleotide repeat expansion, such as Friedreich ataxia (FA) and fragile X syndrome, can result in reduced gene expression and deficiency of vital proteins; in other diseases, such as myotonic dystrophy type-1 (DM1), Fuchs endothelial corneal dystrophy (FECD), and Huntington disease, the nucleotide repeat expansions result in the generation of toxic gene products, often associated with pathological nuclear foci and broad splicing disruptions. Our GeneTAC™ small molecules are designed to selectively target expanded genetic repeat sequences, modulate gene expression either by dialing up or down mRNA transcription, depending on the cause of the disease, and restore cellular health. As a platform, we believe that GeneTAC™ molecules have broad potential applicability across currently unaddressed degenerative, monogenic nucleotide repeat expansion diseases affecting millions of individuals worldwide.

In preclinical studies for our lead program in FA, we have observed restoration of frataxin (FXN) levels in multiple cell types from FA patients and an *in vivo* murine model of FA using our FA GeneTAC™ molecules. At doses that were observed to be well tolerated in rodents and non-human primates, FA GeneTAC™ molecules achieved biodistribution to brain and heart, key organs affected by FA, at concentrations that exceeded those observed to restore FXN levels in FA patient cells. Further, and consistent with this favorable target-organ biodistribution, we observed increased endogenous FXN expression in the brain and heart in an animal model of FA after treatment with our FA GeneTAC™ molecules. In February 2022, the Investigational New Drug Application (IND) for our lead FA GeneTAC™ development candidate (DT-216) was cleared by the U.S. Food and Drug Administration (FDA). Additionally, the FDA has granted Fast Track designation to DT-216 for the treatment of patients with FA. In March 2022, we completed dosing in the first cohort for the single-ascending dose (SAD) Phase 1 clinical trial of DT-216. In December 2022, we reported positive initial data from the SAD clinical trial showing that DT-216 was generally well-tolerated and able to overcome the FXN transcription impairment that causes FA, with a greater than two-fold increase in FXN mRNA in the cohort with the highest response. These data support the continued advancement of DT-216 in the ongoing multiple-ascending dose Phase 1 clinical trial of DT-216 and the anticipated Phase 2 clinical trial in FA patients, which is expected to begin in the second half of 2023.

In December 2022, we nominated our second GeneTAC™ development candidate (DT-168), an eye drop for the treatment of FECD. When tested *in vitro* in FECD patient-derived corneal endothelial cells, our FECD GeneTAC™ molecules led to robust reductions in the pathogenic nuclear RNA foci and corrected key mis-spliced transcripts to levels observed in control corneal endothelial cells from unaffected donors. DT-168 was well tolerated and distribution of DT-168 was observed in and through the cornea in animal models after administration via eye drop. We believe these preclinical data support the potential of our novel GeneTAC™ small molecules to correct the most common underlying genetic cause of FECD, and we plan to advance this research program through additional preclinical studies and submit an IND for DT-168 in the second half of 2023.

Our third program based on the GeneTAC™ platform is DM1. Multiple DM1 GeneTAC™ molecules elicited robust reduction of nuclear foci and correction of splicing defects in DM1 patient muscle cells. Preclinical *in vivo* studies demonstrated distribution of DM1 GeneTAC™ molecules to key target tissues including skeletal muscle and heart, achieving tissue concentrations of intact DM1 GeneTAC™ molecule that reduced pathogenic nuclear foci to normal levels in our *in vitro* experiments. We expect to complete IND-enabling studies and submit an IND in 2024.

To date, we have incurred net losses and negative cash flows from operations since our inception and as of December 31, 2022, had an accumulated deficit of \$110.8 million. Our net losses have resulted primarily from costs incurred in connection with organizing and staffing our company, business planning, raising capital, developing and optimizing our technology platform, identifying potential product candidates, undertaking research and preclinical studies, clinical development activities, engaging in manufacturing for our development programs, and providing general and administrative support for these operations. We do not have any products approved for sale and have not generated any revenue from product sales.

We expect our expenses and operating losses will increase substantially for the foreseeable future as we continue to conduct preclinical studies and clinical trials for our product candidates, nominate additional product candidates from our discovery programs, and as we expand our clinical, regulatory, quality and manufacturing capabilities, incur significant commercialization expenses for marketing, sales, manufacturing and distribution, if we obtain marketing approval for any of our product candidates, and incur additional costs associated with operating as a public company.

We have funded our operations primarily through the sale of our common stock, convertible preferred stock, grant revenue and the issuance of convertible notes and debt. In March 2021, we completed our initial public offering in which we sold 13,800,000 shares of our common stock at \$20.00 per share and received net proceeds, after underwriting discount and offering costs, of \$254.3 million. In January 2021, we issued 19,083,979 shares of Series B convertible preferred stock at \$6.55 per share for net proceeds of approximately \$124.7 million. Our cash, cash equivalents and investment securities balance as of December 31, 2022, was \$330.4 million.

Components of Our Results of Operations

Research and Development Expenses

To date, our research and development expenses have consisted primarily of direct and indirect costs incurred in connection with the clinical development, preclinical development and manufacturing of our product candidates and our discovery efforts. 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 are capitalized until the goods or services are received.

Direct costs include:

- external research and development expenses incurred under agreements with contract research organizations, consultants and other vendors that conduct our clinical, preclinical and discovery activities;
- expenses related to manufacturing our product candidates for clinical and preclinical studies;
- laboratory supplies; and
- license fees.

Indirect costs include:

- personnel-related expenses, consisting of employee salaries, payroll taxes, bonuses, benefits and stock-based compensation charges for those individuals involved in research and development efforts; and
- facilities expenses which include allocated expenses for amortization of right-of-use (ROU) assets, depreciation and other overhead expenses, costs for general laboratory consumables and other indirect expenses.

A significant portion of our research and development expenses have been direct costs, which we track by stage of development, preclinical or clinical. However, we do not track our internal research and development expenses on a program specific basis, because these costs are deployed across multiple projects and, as such, are not separately classified.

We expect that our research and development expenses will substantially increase for the foreseeable future as we continue the development of our FA program, FECD program, DM1 program and our other discovery programs, in particular as we advance our product candidates into clinical development. As of the date of this Annual Report, we cannot reasonably determine with certainty the timing of initiation, the duration or the completion costs of current or future preclinical studies and clinical programs of our product candidates due to the inherently unpredictable nature of preclinical and clinical development. Preclinical and clinical development timelines, the probability of success and development costs can differ materially from expectations. We anticipate that we will make determinations as to which product candidates to pursue and how much funding to direct to each product candidate on an ongoing basis in response to the results of ongoing and future preclinical studies and clinical trials, regulatory developments and our ongoing assessments as to each product candidate's commercial potential. We will need to raise substantial additional capital in the future. In addition, we cannot forecast which product candidates may be subject to future collaborations, when such arrangements will be secured, if at all, and to what degree such arrangements would affect our development plans and capital requirements.

Our future research and development expenses may vary significantly based on a wide variety of factors such as:

- the number and scope, rate of progress, expense and results of our discovery and preclinical development activities;
- 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;
- potential additional safety monitoring requested by regulatory agencies;
- the duration of patient participation in the trials and follow-up;
- the phase of development of the product candidate;
- the efficacy and safety profile of the product candidate;
- the timing, receipt, and terms of any approvals from applicable regulatory authorities including FDA and non-U.S. regulators;
- maintaining a continued acceptable safety profile of our product candidates following approval, if any, of our product candidates;
- establishing clinical or commercial manufacturing capabilities or making arrangements with third-party manufacturers in order to ensure that we or our third-party manufacturers are able to make product successfully;
- significant and changing government regulation and regulatory guidance;

- the impact of any business interruptions to our operations or to those of the third parties with whom we work; and
- the extent to which we establish additional strategic collaborations or other arrangements.

A change in the outcome of any of these variables with respect to the development of any of our product candidates could significantly change the costs and timing associated with the development of that product candidate.

The process of conducting the necessary preclinical and clinical research to obtain regulatory approval is costly and time-consuming. The actual probability of success for our product candidates or any future candidates may be affected by a variety of factors. We may never succeed in achieving regulatory approval for any of our product candidates or any future candidates. Further, a number of factors, including those outside of our control, could adversely impact the timing and duration of our product candidates' or any future candidates' development, which could increase our research and development expenses.

General and Administrative

General and administrative expenses consist primarily of personnel-related expenses, including employee salaries, bonuses, benefits, and stock-based compensation charges, for personnel in executive and administrative functions. Other significant general and administrative expenses include insurance costs, legal fees relating to intellectual property and corporate matters and professional fees for accounting, tax and consulting services.

We anticipate that our general and administrative expenses will substantially increase in the foreseeable future as we add general and administrative personnel to support our expanded research and development activities and infrastructure and, if any of our product candidates or any future candidates receive marketing approval, commercialization activities, as well as to support our operations generally, including facility-related expenses and patent-related costs. We also expect to incur increased expenses related to accounting, audit, legal, regulatory and tax-related services, director and officer insurance premiums, board of director fees, investor and public relations, and other costs associated with operating as a public company.

Results of Operations

Comparison of the Years Ended December 31, 2022 and 2021

The following table summarizes our operating expenses for the years ended December 31, 2022 and 2021 (in thousands):

	Year Ended December 31,		Change
	2022	2021	
Operating expenses:			
Research and development	\$ 48,613	\$ 24,778	\$ 23,835
General and administrative	18,980	11,053	7,927
Total operating expenses	<u>\$ 67,593</u>	<u>\$ 35,831</u>	<u>\$ 31,762</u>

Research and Development Expenses. Research and development expenses were \$48.6 million and \$24.8 million for the years ended December 31, 2022 and 2021, respectively. The increase of \$23.8 million in research and development expenses was due primarily to the advancement of our FA program, including clinical development costs, and additional expenses to support our early-stage programs, during the year ended December 31, 2022. In addition, we incurred higher personnel and related costs during the year ended December 31, 2022 as compared to the same period in 2021, as we expanded the number of research and development employees to support our programs. The increased personnel related costs include an additional \$3.0 million of non-cash stock-based compensation costs incurred during 2022 as compared to 2021.

The following table summarizes our research and development expenses by direct and indirect costs for the year ended December 31, 2022 and 2021 (in thousands):

	Year Ended December 31,		Change
	2022	2021	
FA DT-216	\$ 16,904	\$ —	\$ 16,904
Other direct	8,583	14,683	(6,100)
Indirect	23,126	10,095	13,031
Total research and development expenses	<u>\$ 48,613</u>	<u>\$ 24,778</u>	<u>\$ 23,835</u>

General and Administrative Expenses. General and administrative expenses were \$19.0 million and \$11.1 million for the years ended December 31, 2022 and 2021, respectively. The increase of \$7.9 million in general and administrative expenses was primarily due to additional personnel and related costs incurred during the year ended December 31, 2022 as compared to the same period in 2021. The increased personnel related costs include an additional \$3.2 million of non-cash stock-based compensation costs incurred during 2022 as compared to 2021. In addition, we incurred increased costs to operate as a public company during the year ended December 31, 2022 as compared to the same period in 2021.

Liquidity and Capital Resources

We have incurred net losses and negative cash flows from operations since our inception and anticipate we will continue to incur net losses for the foreseeable future. Since our inception, we have funded our operations primarily through the sale of our common stock, convertible preferred stock, grant income and the issuance of convertible notes and notes payable. In March 2021, we completed our initial public offering in which we sold 13,800,000 shares of our common stock at \$20.00 per share and received net proceeds, after underwriting discount and offering costs, of \$254.3 million. In January 2021, we issued 19,083,979 shares of Series B convertible preferred stock at \$6.55 per share for net proceeds of approximately \$124.7 million.

As of December 31, 2022, we had \$330.4 million of combined cash and cash equivalents and investment securities, a decrease of \$53.7 million from the \$384.1 million of cash and cash equivalents and investment securities at December 31, 2021. This decrease is primarily due to cash used in operations to advance our FA program as well as our early-stage programs. The decrease of \$272.1 million in cash and cash equivalents for the year ended December 31, 2022 was primarily due to investment securities purchased in addition to cash used in operations. Further detail of the change in our cash and cash equivalents for the year ended December 31, 2022 and 2021 is summarized below (in thousands):

	Year Ended December 31,		Change
	2022	2021	
Net cash (used in) provided by:			
Operating activities	\$ (51,317)	\$ (29,377)	\$ (21,940)
Investing activities	(220,987)	(53,644)	(167,343)
Financing activities	235	379,211	(378,976)
Net (decrease) increase in cash and cash equivalents	<u>\$ (272,069)</u>	<u>\$ 296,190</u>	<u>\$ (568,259)</u>

Operating Activities. Net cash used in operating activities was \$51.3 million and \$29.4 million for the years ended December 31, 2022 and 2021, respectively. The increase in our use of cash was primarily due to the increase in net loss from \$35.5 million for the year ended December 31, 2021 to \$63.3 million for the year ended December 31, 2022, a \$27.8 million increase. The higher net loss incurred during the 2022 period was due primarily to the advancement of our FA program as well as increased expense related to our early-stage programs, and higher personnel costs to support these activities, including \$6.2 million of increased non-cash stock-based compensation.

Investing Activities. Net cash used in investing activities was \$221.0 million and \$53.6 million for the years ended December 31, 2022 and 2021, respectively. The increase in cash used in investing activities was primarily due to increased purchases of investment securities during the year ended December 31, 2022, as compared to the same period in 2021. We have classified our investments securities as available-for-sale and all investments are made in accordance with our investment policy.

Financing Activities. Net cash provided by financing activities was \$0.2 million for the year ended December 31, 2022 from the proceeds received from employee stock option exercises and issuance of common stock through our employee stock purchase plan, partially offset by the payment of deferred issuance costs. Net cash provided by financing activities was \$379.2 million for the year ended December 31, 2021, from the \$254.3 million of net proceeds received from our initial public offering in March 2021 and the \$124.7 million of net proceeds received from the closing of our Series B convertible preferred stock financing in January 2021.

Shelf Registration Statement

In April 2022, we filed a shelf registration statement on Form S-3 (2022 Shelf Registration Statement), which became effective in May 2022. The 2022 Shelf Registration Statement permits: (i) the offering, issuance and sale by us of up to a maximum aggregate offering price of \$300.0 million of common stock, preferred stock, debt securities and warrants in one or more offerings and in any combination; and (ii) the offering, issuance and sale by us of up to a maximum aggregate offering price of \$100.0 million of our common stock that may be issued and sold under an "at-the-market" sales agreement (ATM Program). The \$100.0 million of common stock that may be issued and sold under the ATM Program is included in the \$300.0 million of securities that may be issued and sold under the 2022 Shelf Registration Statement.

Funding Requirements

Based on our current operating plan, we believe that our existing cash, cash equivalents and investments will be sufficient to fund our planned operating expenses and capital expenditure requirements for more than the next 12 months following the date of this Annual Report.

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 expend our capital resources sooner than we expect. Additionally, the process of testing product candidates in clinical trials is costly, and the timing of progress and expenses in these trials is uncertain.

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

- the scope, rate of progress and costs of our drug discovery, preclinical development activities and clinical trials for any product candidates;
- the number and scope of clinical programs we decide to pursue;
- the scope and costs of manufacturing our product candidates and any future commercial manufacturing activities;
- the emergence of competing therapies and other adverse market developments;
- the cost, timing and outcome of seeking FDA, EMA and any other regulatory approvals for any product candidates;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;
- the terms and timing of establishing and maintaining strategic collaborations, licenses and other similar arrangements and the financial terms of such agreements;
- our efforts to enhance operational systems and our ability to attract, hire and retain qualified personnel, including personnel to support the development of our product candidates;
- the costs associated with being a public company;

- the timing of any milestone and royalty payments to Wisconsin Alumni Research Foundation (WARF), or other future licensors;
- the extent to which we acquire or in-license other product candidates and technologies;
- our need and ability to retain key management and hire scientific, technical, business, and medical personnel;
- our implementation of additional internal systems and infrastructure, including operational, financial and management information systems;
- the costs associated with expanding our facilities or building out our additional laboratory space;
- the effects of the recent disruptions to and volatility in the credit and financial markets as a result of macroeconomic factors; and
- the cost associated with commercialization activities for any of our current or future product candidates, if approved.

Until such time, if ever, as we can generate substantial revenues from product sales to support our cost structure, we expect to finance our cash needs through public or private equity offerings, debt financings, or other capital sources which may include strategic collaborations, licensing arrangements or other arrangements with third parties. 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. Equity and debt 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 strategic collaborations, or other similar 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 and/or may reduce the value of our common stock. 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 drug development or future commercialization efforts. Our ability to raise additional funds may be adversely impacted by potential worsening global economic conditions and disruptions to and volatility in the credit and financial markets in the United States and worldwide as a result of macroeconomic factors, including geopolitical conflicts, high inflation, global supply chain challenges, and the effects of a resurgence of COVID-19 or other health epidemic or pandemic. Because of the numerous risks and uncertainties associated with product development, we cannot predict the timing or amount of increased expenses and cannot assure you that we will ever be profitable or generate positive cash flow from operating activities.

Contractual Obligations, Commitments and Material Cash Requirements

In February 2021, we entered into a lease agreement to rent approximately 12,370 square feet of lab and office space with a related party. The delivery date of the space was September 1, 2021, and the lease commenced at that time. The term of the lease is 72 months after commencement with an option to extend the lease term for a period of three years. Annual rent payments will be approximately \$0.8 million per year, subject to annual increases of 3%, plus our share of operating expenses and taxes.

In March 2022, we entered into an amendment to our existing lease agreement to rent approximately 4,900 square feet of additional space with a related party. The delivery date of the space was June 16, 2022, and the lease amendment commenced at that time. The term of the lease coincides with our existing lease. Annual rent payments for the additional space will be approximately \$0.1 million, subject to annual increases of 3%, plus our share of operating expenses and taxes.

In February 2019, we entered into a Human Therapeutics Exclusive License Agreement (License Agreement) with the Wisconsin Alumni Research Foundation (WARF). Under the License Agreement, we licensed the exclusive, worldwide, royalty-bearing, sublicensable rights to certain WARF patents and the nonexclusive worldwide rights to certain know-how to develop and commercialize products for the prevention, diagnosis and treatment of disease. As consideration for the license, we agreed to pay an upfront fee of \$0.3 million, which we immediately expensed as a research and development expense in our statements of operations as there was no alternative future use for the license.

For the year ended December 31, 2022, pursuant to the License Agreement, we paid \$0.1 million to WARF upon the acceptance of an IND in the U.S. and will be required to make further aggregate milestone payments of up to \$17.5 million upon achievement of certain other regulatory and commercial milestones. We may also be required to pay royalties based on annual net product sales in the low single digits on our or our sublicensees' net product sales on a country-by-country and product-by-product basis, and are subject to a minimum royalty of \$0.1 million per calendar year upon first commercial product sale. Further, we may be required to pay sublicense fees in the mid-single digits percentage for fees, royalties or other payments earned from the granting of sublicenses to the WARF patents and know-how.

We are responsible for reimbursing WARF for costs incurred in connection with prosecuting and maintaining patent rights that are specific to the License Agreement. Expenses recognized in connection with legal patent fees under this License Agreement were immaterial for the years ended December 31, 2022 and 2021, respectively.

We may terminate the License Agreement with 90 days written notice or for certain breaches of the agreement. WARF may terminate the License Agreement with 90 days written notice if first commercial sale does not occur before December 31, 2031. Unless terminated earlier by the parties, the term of the License Agreement will continue until the last licensed patent expires in all countries.

Additionally, we enter into agreements in the normal course of business with third-party vendors for preclinical studies, clinical trial related services, research supplies and other services and products for operating purposes. These contracts generally provide for termination following a certain period after notice and therefore we believe that our non-cancelable obligations under these agreements are not material.

In addition to the contractual obligations above, we also expect to have future material cash requirements related to our ongoing and planned clinical trials, discovery and preclinical programs, personnel and facilities-related expenses, external research and development and product development.

Critical Accounting Policies and Significant Judgments and Estimates

Our management's discussion and analysis of our financial condition and results of operations are based on our financial statements, which have been prepared in accordance with U.S. generally accepted accounting principles. The preparation of these financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, revenue and expenses and the disclosure of contingent assets and liabilities in our financial statements. On an ongoing basis, we evaluate our estimates and judgments, including those related to grant revenue and research and development expenses. We base our estimates on historical experience, known trends and events, and various other factors that are believed to be 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. Actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies and estimates are described in more detail in Note 2 to our audited financial statements appearing in Part II, Item 8 of this Annual Report on Form 10-K, we believe the following accounting policies and estimates to be most critical to the preparation of our financial statements.

Accrued Research and Development Expenses

As part of the process of preparing our financial statements as of each balance sheet date, we are required to estimate our accrued expenses resulting from obligations under contracts with third-party vendors, contract research organizations (CROs) and consultants, in connection with research and development activities and conducting clinical trials. This process involves reviewing open contracts and purchase orders, communicating with our personnel and outside vendors to identify services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of the actual cost. We make estimates of our accrued expenses as of each balance sheet date based on facts and circumstances known to us at that time. The accruals are dependent upon accurate reporting by CROs and other third-party vendors. We periodically confirm the accuracy of our estimates with the service providers and make adjustments if necessary. The significant estimates in our accrued research and development expenses include the costs incurred for services performed by our vendors in connection with research and development activities and clinical trials for which we have not yet been invoiced. Since our inception, we have not experienced any material differences between accrued or prepaid costs and actual costs.

We base our expenses related to research and development and clinical trial activities on our estimates of the services received and efforts expended pursuant to quotes and contracts with vendors that conduct these activities on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the research and development expense. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrual or prepaid expense accordingly. Advance payments for goods and services that will be used in future research and development activities are expensed when the activity has been performed or when the goods have been received rather than when the payment is made.

Recent Accounting Pronouncements

See Item 8 of Part II, “Notes to Financial Statements — Note 2 — Basis of Presentation and Summary of Significant Accounting Policies” for a discussion of recent accounting pronouncements.

Other Information

Emerging Growth Company Status

We are an emerging growth company, as defined in the Jumpstart Our Business Startups Act, as amended (JOBS Act), and we may remain an emerging growth company until as late as December 31, 2026 (the fiscal year-end following the fifth anniversary of the completion of our initial public offering). For so long as we remain an emerging growth company, we are permitted and intend to rely on certain exemptions from various public company reporting requirements, including not being required to have our internal control over financial reporting audited by our independent registered public accounting firm pursuant to Section 404 of the Sarbanes-Oxley Act, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements, and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and any golden parachute payments not previously approved.

Under the JOBS Act, emerging growth companies can delay adopting new or revised accounting standards issued subsequent to the enactment of the JOBS Act until such time as those standards apply to private companies. We have irrevocably elected not to avail ourselves of this exemption from new or revised accounting standards and, therefore, will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

We will remain an emerging growth company until the earliest to occur of: (i) the last day of the fiscal year in which we have at least \$1.235 billion in annual revenue; (ii) the date upon which we are deemed to be a “large accelerated filer,” as defined in Rule 12b-2 under the Exchange Act, which would occur if we have been subject to the reporting requirements of the Exchange Act for at least 12 months as of December 31st and the market value of our common stock held by non-affiliates exceeded \$700.0 million as of the last business day of the second fiscal quarter of such year; (iii) the date on which we have issued more than \$1.0 billion in nonconvertible debt securities during the prior three-year period; and (iv) December 31, 2026 (the last day of the fiscal year ending after the fifth anniversary of our initial public offering).

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

As a "smaller reporting company," we are not required to provide the information otherwise required by this item.

Item 8. Financial Statements and Supplementary Data.

INDEX TO FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm (PCAOB ID: 42)	F-2
Balance Sheets as of December 31, 2022 and 2021	F-3
Statements of Operations for the Years ended December 31, 2022 and 2021	F-4
Statements of Comprehensive Loss for the Years Ended December 31, 2022 and 2021	F-5
Statements of Stockholders' Equity for the Years ended December 31, 2022 and 2021	F-6
Statements of Cash Flows for the Years ended December 31, 2022 and 2021	F-7
Notes to Financial Statements	F-8

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Design Therapeutics, Inc.

Opinion on the Financial Statements

We have audited the accompanying balance sheets of Design Therapeutics, Inc. (the Company) as of December 31, 2022 and 2021, the related statements of operations, comprehensive loss, convertible preferred stock and stockholders' equity and cash flows for each of the two years in the period ended December 31, 2022, and the related notes (collectively referred to as the "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2022 and 2021, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2022, in conformity with U.S. generally accepted accounting principles.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2020.

San Diego, California
March 14, 2023

Design Therapeutics, Inc.
Balance Sheets
(in thousands, except share and par value data)

	December 31, 2022	December 31, 2021
Assets		
Current assets:		
Cash and cash equivalents	\$ 26,500	\$ 298,569
Investment securities	303,887	85,495
Prepaid expenses and other current assets	4,732	1,371
Total current assets	335,119	385,435
Property and equipment, net	1,947	1,508
Right-of-use asset, related party	3,612	3,614
Other assets	459	—
Total assets	<u>\$ 341,137</u>	<u>\$ 390,557</u>
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	\$ 3,025	\$ 1,620
Accrued expenses and other current liabilities (including related party amounts of \$640 and \$504, respectively)	7,751	3,663
Total current liabilities	10,776	5,283
Operating lease liability, net, related party	3,051	3,144
Total liabilities	<u>13,827</u>	<u>8,427</u>
Commitments and contingencies (See Note 11)		
Stockholders' equity:		
Common stock: \$0.0001 par value; 200,000,000 shares authorized, 55,943,314 and 55,681,752 shares issued, and 55,895,596 and 55,441,926 shares outstanding at December 31, 2022 and 2021, respectively	6	6
Additional paid-in capital	441,424	429,824
Accumulated deficit	(110,764)	(47,456)
Accumulated other comprehensive loss	(3,356)	(244)
Total stockholders' equity	327,310	382,130
Total liabilities and stockholders' equity	<u>\$ 341,137</u>	<u>\$ 390,557</u>

The accompanying notes are an integral part of these financial statements.

Design Therapeutics, Inc.
Statements of Operations
(in thousands, except share and per share data)

	<u>Year Ended December 31,</u>	
	<u>2022</u>	<u>2021</u>
Operating expenses:		
Research and development (including related party amounts of \$960 and \$405, respectively)	48,613	24,778
General and administrative (including related party amounts of \$530 and \$328, respectively)	18,980	11,053
Total operating expenses	<u>67,593</u>	<u>35,831</u>
Loss from operations	(67,593)	(35,831)
Other income, net	4,285	298
Net loss	<u>\$ (63,308)</u>	<u>\$ (35,533)</u>
Net loss per share, basic and diluted	<u>\$ (1.14)</u>	<u>\$ (0.77)</u>
Weighted-average shares of common stock outstanding, basic and diluted	<u>55,707,517</u>	<u>45,936,235</u>

The accompanying notes are an integral part of these financial statements.

Design Therapeutics, Inc.
Statements of Comprehensive Loss
(in thousands, except share and per share data)

	Year Ended December 31,	
	2022	2021
Net loss	\$ (63,308)	\$ (35,533)
Other comprehensive loss:		
Unrealized loss on available-for-sale securities	(3,112)	(400)
Comprehensive loss	\$ (66,420)	\$ (35,933)

The accompanying notes are an integral part of these financial statements.

Design Therapeutics, Inc.
Statements of Convertible Preferred Stock and Stockholders' Equity
(in thousands, except share data)

	Convertible Preferred Stock		Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Stockholders' Equity (Deficit)
	Shares	Amount	Shares	Amount				
Balance at December 31, 2020	22,012,499	\$ 45,356	15,957,821	\$ 1	\$ 451	\$ 156	\$ (11,923)	\$ (11,315)
Issuance of Series B convertible preferred stock, net of \$288 of issuance costs	19,083,979	124,712	—	—	—	—	—	—
Preferred stock converted into shares of common stock	(41,096,478)	(170,068)	25,212,548	4	170,064	—	—	170,068
Initial public offering of common shares, net of \$21,728 of issuance costs	—	—	13,800,000	1	254,270	—	—	254,271
Exercises of stock options and vesting of restricted stock	—	—	460,101	—	156	—	—	156
Issuance of common stock under employee stock purchase plan	—	—	11,456	—	194	—	—	194
Stock-based compensation	—	—	—	—	4,689	—	—	4,689
Unrealized loss on investments	—	—	—	—	—	(400)	—	(400)
Net loss	—	—	—	—	—	—	(35,533)	(35,533)
Balance at December 31, 2021	—	\$ —	55,441,926	\$ 6	\$ 429,824	\$ (244)	\$ (47,456)	\$ 382,130
Exercises of stock options and vesting of restricted stock	—	—	418,236	—	336	—	—	336
Issuance of common stock under employee stock purchase plan	—	—	35,434	—	339	—	—	339
Stock-based compensation	—	—	—	—	10,925	—	—	10,925
Unrealized loss on investments	—	—	—	—	—	(3,112)	—	(3,112)
Net loss	—	—	—	—	—	—	(63,308)	(63,308)
Balance at December 31, 2022	—	\$ —	55,895,596	\$ 6	\$ 441,424	\$ (3,356)	\$ (110,764)	\$ 327,310

The accompanying notes are an integral part of these financial statements.

Design Therapeutics, Inc.
Statements of Cash Flows
(in thousands)

	<u>Year Ended December 31,</u>	
	<u>2022</u>	<u>2021</u>
Cash flows from operating activities		
Net loss	\$ (63,308)	\$ (35,533)
Reconciliation of net loss to net cash used in operating activities:		
Depreciation	406	129
Stock-based compensation	10,925	4,689
Amortization of premiums on investment securities, net	(1,396)	(77)
Non-cash lease expense	60	19
Other	4	—
Change in operating assets and liabilities:		
Prepaid expense and other assets	(3,393)	(1,017)
Accounts payable and other liabilities	5,400	2,418
Accounts payable and other liabilities—related party	(15)	(5)
Net cash used in operating activities	<u>(51,317)</u>	<u>(29,377)</u>
Cash flows from investing activities		
Purchases of investment securities	(312,998)	(86,261)
Proceeds from maturities of investment securities	92,890	34,155
Proceeds from sale of asset	39	—
Purchases of property and equipment	(918)	(1,538)
Net cash used in investing activities	<u>(220,987)</u>	<u>(53,644)</u>
Cash flows from financing activities		
Proceeds from initial public offering, net of issuance costs	—	254,271
Proceeds from issuance of convertible preferred stock, net of issuance costs	—	124,712
Payment of deferred issuance costs	(427)	—
Issuance of common stock through employee stock purchase plan	339	194
Proceeds from the exercise of stock options	323	34
Net cash provided by financing activities	<u>235</u>	<u>379,211</u>
Net (decrease) increase in cash and cash equivalents	(272,069)	296,190
Cash and cash equivalents at beginning of period	298,569	2,379
Cash and cash equivalents at end of period	<u>\$ 26,500</u>	<u>\$ 298,569</u>
Supplemental disclosures		
Initial recognition of operating lease right-of-use asset and operating lease liability	<u>\$ 590</u>	<u>\$ 3,786</u>
Purchases of property and equipment included in accrued expenses	<u>\$ —</u>	<u>\$ 29</u>

The accompanying notes are an integral part of these financial statements.

Design Therapeutics, Inc.
Notes to Financial Statements

1. Organization

Design Therapeutics, Inc. (the "Company") was incorporated in Delaware in December 2017 and is based in Carlsbad, California. The Company is a clinical-stage biopharmaceutical company pioneering the research and development of GeneTAC™ molecules, which are a novel class of small-molecule gene targeted chimera therapeutic candidates designed to be disease-modifying by addressing the underlying cause of diseases caused by inherited nucleotide repeat expansion mutations. The Company's lead product candidate is in Friedreich ataxia ("FA"), its second product candidate is in Fuchs Endothelial Corneal Dystrophy ("FECD"), and it is also advancing its GeneTAC™ program to address other serious nucleotide repeat-driven monogenic diseases.

Stock Splits

In March 2021, the Company effected a 1-for-1.63 reverse stock split of its issued and outstanding common stock. The par value and the authorized shares of the common stock were not adjusted as a result of these stock splits. The reverse stock split in March 2021 resulted in an adjustment to the convertible preferred stock conversion prices to reflect a proportional decrease in the number of shares of common stock to be issued upon conversion. The accompanying financial statements and notes to the financial statements give retroactive effect to the stock splits for all periods presented.

Initial Public Offering

In March 2021, the Company completed its initial public offering ("IPO") selling 13,800,000 shares of its common stock at \$20.00 per share. Proceeds from the Company's IPO, net of underwriting discounts and commissions and other offering costs, were \$254.3 million. In connection with the IPO, all 41,096,478 shares of convertible preferred stock outstanding at the time of the IPO converted into 25,212,548 shares of the Company's common stock.

Liquidity and Capital Resources

The accompanying financial statements have been prepared assuming that the Company will continue as a going concern, which contemplates the realization of assets and the satisfaction of liabilities in the normal course of business. The Company has incurred net operating losses since inception and had an accumulated deficit of \$110.8 million as of December 31, 2022. The Company had cash, cash equivalents and investment securities of \$330.4 million as of December 31, 2022, and has not generated positive cash flow from operations.

Management expects to incur net losses for the foreseeable future. There can be no assurance that the Company will ever earn revenues or achieve profitability, or if achieved, that they will be sustained on a continuing basis. In addition, the research, product development, and clinical development activities as well as the commercialization of the Company's products, if approved, will require significant additional financing. The Company may be unable to secure such financing when needed, or if available, such financings may be under terms that are unfavorable to the Company or the current stockholders. If the Company is unable to raise additional funds when needed, it may be required to delay, reduce the scope of, or eliminate development programs, which may adversely affect its business and operations. The Company's currently available cash and cash equivalents as of December 31, 2022 are sufficient to meet its anticipated cash requirements for more than 12 months following the date the financial statements are issued.

2. Basis of Presentation and Summary of Significant Accounting Policies

Basis of Presentation and Use of Estimates

The financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America (GAAP). The preparation of financial statements in conformity with GAAP requires the Company to make estimates and assumptions that impact the reported amounts of assets, liabilities, revenues and

expenses and the disclosure of contingent assets and liabilities in the financial statements and accompanying notes. Although these estimates are based on the Company's knowledge of current events and anticipated actions it may undertake in the future, actual results may ultimately materially differ from these 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 in making decisions regarding resource allocation and assessing performance. The Company manages its operations as a single reportable segment for the purposes of assessing performance and making operating decisions.

Concentrations of Credit Risk

Financial instruments that potentially subject the Company to significant concentrations of credit risk consist primarily of cash, cash equivalents and investment securities. The Company maintains deposits in federally insured financial institutions in excess of federally insured limits. The Company has not experienced any losses in such accounts and believes it is not exposed to significant risk on its cash balances due to the financial position of the depository institution in which those deposits are held. Additionally, the Company has established guidelines regarding approved investments and maturities of investments, which are designed to maintain safety and liquidity.

Cash and Cash Equivalents

The Company considers all highly liquid investments with maturities at the date of acquisition of three months or less to be cash equivalents. These investments may include money market accounts, money market funds, U.S. Government agency securities, corporate debt securities and commercial paper. The carrying amounts approximate fair value due to the short maturities of these instruments. The Company's cash reserves are in a readily available checking account.

Investment Securities

Investments in securities with maturities at the date of acquisition of more than three months are considered marketable securities. These investments may include money market accounts, money market funds, certificates of deposits, U.S. Treasury securities and high quality, marketable debt instruments of corporations and government sponsored enterprises. The Company determines the appropriate classification of its investments at the time of acquisition and reevaluates such determination at each balance sheet date. The Company has classified its investment holdings as available-for-sale, as the sale of such securities may be required prior to maturity to implement management strategies. Further, the Company classifies its available-for-sale investment securities, including those with maturities beyond one year, as current assets on its balance sheets based on the highly liquid nature of the securities and because these investments are considered available for use in current operations. The Company's investment policy sets minimum credit quality criteria and maximum maturity limits on its investments to provide for safety of principle, liquidity and a reasonable rate of return. Available-for-sale securities are recorded at fair value, based on current market valuations. Unrealized holding gains and losses on available-for-sale securities are excluded from earnings and are reported as a separate component of other comprehensive income (loss) until realized. Allowances for credit losses are reported on the balance sheet, if any.

The cost of available-for-sale investment securities is adjusted for amortization of premiums and accretion of discounts until the securities mature. Such amortization and accretion is included in other income, net on the statements of operations. Realized gains and losses, if any, are also included in other income, net on the statement of operations and are derived using the specific identification method for determining the cost of the securities sold. During the periods presented, no realized gains or losses were recorded on the sale of investment securities and no impairments to reduce the value of any security was taken. See Note 5 for further discussion.

Property and Equipment, Net

Property and equipment generally consist of laboratory equipment, computer equipment and software, and furniture and fixtures and are recorded at cost and depreciated using the straight-line method over the estimated useful lives of the assets (generally three to five years). Leasehold improvements are recorded at cost and are

depreciated on a straight-line basis over the lesser of the remaining term of the related lease or the estimated useful lives of the assets. Repairs and maintenance costs are charged as incurred.

An impairment loss is recorded if and when events and circumstances indicate that assets might be impaired and the undiscounted cash flows estimated to be generated by those assets are less than the carrying amount of those assets. The Company has not recognized any impairment losses for the years ended December 31, 2022 and 2021.

Leases

Leases consist of an operating lease the Company has related to its facility. At lease commencement, the Company records a lease liability based on the present value of lease payments over the expected lease term. The expected lease term includes noncancelable lease periods and, when applicable, periods covered by an option to extend the lease if the Company is reasonably certain to exercise that option, as well as periods covered by an option to terminate the lease if the Company is reasonably certain not to exercise the option. For those leases where the implicit rate is not provided, the Company calculates the present value of lease payments using an incremental borrowing rate. The Company's incremental borrowing rate for a lease is the rate of interest it would have to pay on a collateralized basis to borrow an amount equal to the lease payments under similar terms. At the lease commencement date, the Company records a corresponding right-of-use ("ROU") lease asset based on the lease liability, adjusted for any lease incentives received and any initial direct costs paid to the lessor prior to the lease commencement date. The Company may enter into leases with an initial term of 12 months or less ("Short-Term Leases"). For any Short-Term leases, the Company records the rent expense on a straight-line basis and ROU asset and lease obligations are not recognized. The Company had no Short-Term Leases as of December 31, 2022 or 2021.

After lease commencement, the Company measures its leases as follows: (i) the lease liability based on the present value of the remaining lease payments using the discount rate determined at lease commencement and (ii) the ROU asset based on the remeasured lease liability, adjusted for any unamortized lease incentives received, any unamortized initial direct costs and the cumulative difference between rent expense and amounts paid under the lease agreement. Any lease incentives received and any initial direct costs are amortized on a straight-line basis over the expected lease term. Rent expense is recorded on a straight-line basis over the expected lease term.

Research and Development Expenses

Research and development expenses are charged to expense in the period in which they are incurred and are comprised of the following types of costs incurred in connection with research and development activities and clinical trials: lab supplies and outside services incurred in connection with the Company's early discovery efforts, contract services for clinical trials and related clinical manufacturing costs, salaries and benefits including share-based compensation expense, costs for allocated facilities and depreciation of equipment.

Patent Costs

Costs related to filing and pursuing patent applications are recorded as general and administrative expenses in the statements of operations and expensed as incurred since recoverability of such expenditures is uncertain.

Stock-Based Compensation

Stock options and restricted stock issued pursuant to the Company's 2021 Equity Incentive Plan (the "2021 Plan") and 2018 Equity Incentive Plan (the "2018 Plan"), and option features associated with the rights to purchase shares pursuant to the Company's 2021 Employee Stock Purchase Plan (the "ESPP") are valued using the Black-Scholes option pricing model on the date of grant or subscription period. This option pricing model involves a number of estimates, including the expected lives of the stock options or subscription period, the Company's anticipated stock volatility and interest rates. The Company recognizes the expense for equity awards on a straight-line basis over the requisite service periods of the awards or the number of shares estimated to be issued pursuant to the ESPP. Forfeitures are recognized as they occur.

Income Taxes

The Company uses the asset and liability method of accounting for income taxes. Under this method, deferred tax assets and liabilities are determined based on the difference between the financial reporting and the tax reporting basis of assets and liabilities and are measured using the enacted tax rates and laws that are expected to be in effect when the differences are expected to reverse. The Company provides a valuation allowance against net deferred tax assets unless, based upon the available evidence, it is more likely than not that the deferred tax assets will be realized. When the Company establishes or reduces the valuation allowance against its deferred tax assets, its provision for income taxes will increase or decrease, respectively, in the period such determination is made.

The accounting guidance for uncertainty in income taxes prescribes a recognition threshold and measurement attribute criteria for the financial statement recognition and measurement of tax positions taken or expected to be taken in a tax return. For those benefits to be recognized, a tax position must be more likely than not to be sustained upon examination by taxing authorities based on the technical merits of the position.

3. Net Loss Per Share

Basic net loss per share is computed by dividing the net loss by the weighted-average number of common shares outstanding for the period, without consideration for potentially dilutive securities. Diluted net loss per share is computed by dividing the net loss by the weighted average number of common shares and dilutive common stock equivalents outstanding for the period determined using the treasury-stock and if-converted methods. Dilutive common stock equivalents are comprised of stock options outstanding under the Company's equity incentive plans, restricted common stock subject to repurchase, and employee stock purchase rights under the Company's ESPP, as applicable. 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:

	<u>December 31,</u> <u>2022</u>	<u>December 31,</u> <u>2021</u>
Stock options	5,396,719	2,673,775
Shares subject to repurchase	47,718	239,826
Employee stock purchase plan	7,096	3,833
Total	<u>5,451,533</u>	<u>2,917,434</u>

4. Fair Value Measurements

Accounting guidance defines fair value, establishes a consistent framework for measuring fair value and expands disclosure for each major asset and liability category measured at fair value on either a recurring or non-recurring basis. Fair value is defined as an exit price, representing the amount that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants. As such, fair value is a market-based measurement that should be determined based on assumptions that market participants would use in pricing an asset or liability. As a basis for considering such assumptions, the accounting guidance establishes a three-tier fair value hierarchy, which prioritizes the inputs used in measuring fair value as follows:

- Level 1: Observable inputs such as quoted prices in active markets.
- Level 2: Inputs, other than the quoted prices in active markets that are observable either directly or indirectly.
- Level 3: Unobservable inputs in which there is little or no market data, which require the reporting entity to develop its own assumptions.

The carrying value of the Company's cash, accounts payable and accrued liabilities are considered to be representative of their respective fair values due to the short-term nature of those instruments. The Company's investment securities, which may include money market accounts, money market funds, certificates of deposits, U.S. Treasury securities, and high quality, marketable debt instruments of corporations and government sponsored

enterprises, are measured at fair value in accordance with the fair value hierarchy. None of the Company's non-financial assets or liabilities are recorded at fair value on a non-recurring basis and no transfers between levels have occurred during the periods presented.

The following table summarizes the Company's financial instruments measured at fair value on a recurring basis at December 31, 2022 and 2021 (in thousands):

	Fair Value Measurement at End of Period Using:			
	Total	Quoted Prices In Active Markets For Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
As of December 31, 2022:				
Assets:				
Money market funds ⁽¹⁾	\$ 20,895	\$ 20,895	\$ —	\$ —
Certificates of deposit	7,929	7,929	—	—
U.S. Treasury securities	265,966	265,966	—	—
U.S. Government agency securities	29,992	—	29,992	—
Total	\$ 324,782	\$ 294,790	\$ 29,992	\$ —
As of December 31, 2021:				
Assets:				
Money market funds ⁽¹⁾	\$ 298,114	\$ 298,114	\$ —	\$ —
Certificates of deposit	5,771	5,771	—	—
U.S. Treasury securities	79,724	79,724	—	—
Total	\$ 383,609	\$ 383,609	\$ —	\$ —

⁽¹⁾ Included in cash and cash equivalents on the accompanying balance sheets.

Interest bearing money market accounts and certificates of deposit are valued at amortized cost, which approximates fair value.

5. Investment Securities

The Company's investment policy defines allowable investment securities and establishes guidelines relating to credit quality, diversification, and maturities of its investments to preserve principal and maintain liquidity. In accordance with the Company's investment policy, it has invested funds in marketable securities. The cost, gross unrealized holding gains, gross unrealized holding losses, allowances for credit losses and fair value of available-

for-sale investments by types, maturities and classes of securities at December 31, 2022 and 2021 consisted of the following (in thousands):

As of December 31, 2022						
	Maturity	Amortized Cost	Unrealized Gains	Unrealized Losses	Allowance for Credit Losses	Estimated Fair Market Value
Certificates of deposits	Within 1 year	\$ 4,092	\$ —	\$ (57)	\$ —	\$ 4,035
U.S. Treasury securities	Within 1 year	200,938	4	(2,182)	—	198,760
U.S. Government agency securities	Within 1 year	22,663	—	(84)	—	22,579
Certificates of deposits	1 year to 2 years	3,920	7	(33)	—	3,894
U.S. Treasury securities	1 year to 2 years	68,130	2	(926)	—	67,206
U.S. Government agency securities	1 year to 2 years	7,500	—	(87)	—	7,413
Total		\$ 307,243	\$ 13	\$ (3,369)	\$ —	\$ 303,887

As of December 31, 2021						
	Maturity	Amortized Cost	Unrealized Gains	Unrealized Losses	Allowance for Credit Losses	Estimated Fair Market Value
Certificates of deposits	Within 1 year	\$ 2,896	\$ —	\$ (3)	\$ —	\$ 2,893
U.S. Treasury securities	Within 1 year	15,045	—	(23)	—	15,022
Certificates of deposits	1 year to 2 years	2,887	—	(9)	—	2,878
U.S. Treasury securities	1 year to 2 years	64,911	—	(209)	—	64,702
Total		\$ 85,739	\$ —	\$ (244)	\$ —	\$ 85,495

The Company reviews its investments at each reporting date to identify and evaluate whether a decline in fair value below the amortized cost basis of available-for-sale securities is due to credit-related factors and determines if such unrealized losses are the result of credit losses that require impairment. Factors considered in determining whether an unrealized loss is the result of a credit loss or other factors include the extent to which the fair value is less than the cost basis, any changes to the rating of the security by a rating agency, the financial condition and near-term prospects of the issuer, any historical failure of the issuer to make scheduled interest or principal payments, any adverse legal or regulatory events affecting the issuer or issuer's industry, any significant deterioration in economic condition and the Company's intent and ability to hold the investment for a period of time sufficient to allow for any anticipated recovery in market value.

At December 31, 2022 there were 77 securities in an unrealized loss position. The Company determined that there was no material change in the credit risk of the securities and considered the decline in market value to be primarily attributable to changes in interest rates. Each security remained at a high credit quality rating and the unrealized losses of each security was immaterial. Further, there had been no adverse conditions noted for any of the issuers and Company does not intend to sell any of the securities prior to maturity. As such, an allowance for credit losses has not been recognized. At December 31, 2021, there were 38 securities in an unrealized loss position.

As of December 31, 2022, the Company held 33 domestic certificates of deposit with amortized costs below the Federal Deposit Insurance Corporation ("FDIC") insured limit. Accrued interest receivable on available-for-sale investment securities, included in prepaids and other current assets on the Company's balance sheets, was \$1.1 million and \$0.1 million at December 31, 2022 and 2021, respectively.

6. Balance Sheet Details

Prepaid expenses and other current assets consisted of the following (in thousands):

	December 31, 2022	December 31, 2021
Prepaid expenses	\$ 3,617	\$ 1,261
Interest receivable	1,115	110
Total	<u>\$ 4,732</u>	<u>\$ 1,371</u>

Property and equipment consisted of the following (in thousands):

	December 31, 2022	December 31, 2021
Laboratory equipment	\$ 1,695	\$ 1,148
Computer equipment and software	102	96
Furniture and fixtures	521	292
Leasehold improvements	151	95
Construction in progress	—	11
	<u>2,469</u>	<u>1,642</u>
Less accumulated depreciation	(522)	(134)
Total	<u>\$ 1,947</u>	<u>\$ 1,508</u>

Accrued expenses and other current liabilities consisted of the following (in thousands):

	December 31, 2022	December 31, 2021
Accrued personnel costs	\$ 3,543	\$ 2,152
Accrued research and development costs	2,983	516
Current portion of operating lease liability, related party	640	489
Accrued other	585	506
Total	<u>\$ 7,751</u>	<u>\$ 3,663</u>

7. Leases

In May 2019, the Company entered into an agreement, as subsequently amended, to lease laboratory space pursuant to a three-month, automatically renewing lease. Due to the short-term nature of the lease, it was not included as an operating lease right of use asset nor as an operating lease liability on the Company's balance sheets. The Company terminated the agreement in September 2021.

In February 2021, the Company entered into a lease agreement with Crossing Holdings, LLC to rent approximately 12,370 square feet of laboratory and office space (the "Lease"). The Company's Executive Chairperson, co-founder and member of its board of directors, is the sole member and Manager of Crossing Holdings, LLC. The lease commenced in September 2021 with a term of 72 months and an option to extend the lease term for a period of three years; however, it is not reasonably certain the Company will exercise the option to renew when the lease term ends in 2027, and thus, the incremental term was excluded from the calculation of the ROU asset or lease liability. Lease payments are subject to annual increases of 3% and the Company is responsible for its share of operating expenses and taxes, which are expensed as incurred. In March 2022, the Company entered into an amendment (the "Lease Amendment") to its Lease with Crossing Holdings, LLC to rent approximately 4,900 square feet of additional office space in the same building. The Lease Amendment commenced in June 2022 and the term of the additional premises under the Lease Amendment will coincide with the term of the Lease and end in 2027. As of December 31, 2022, the weighed-average remaining lease term for the Company's leases was 4.7 years and the weighted-average discount rate used to determine the right-of-use asset and corresponding operating lease liability was 7.37%.

Maturities of operating lease liabilities, related party as of December 31, 2022 are as follows (in thousands):

2023	\$	891
2024		918
2025		945
2026		974
2027		663
Thereafter		—
Total future minimum lease payments		4,391
Less: Present value adjustment		(700)
Operating lease liabilities, related party	\$	<u>3,691</u>

Rent expense for the years ended December 31, 2022 and 2021 was \$0.9 million and \$0.6 million, respectively.

8. Convertible Preferred Stock and Stockholders' Deficit

Authorized Shares

In connection with the completion of the Company's IPO in March 2021, the Company amended its Certificate of Incorporation to authorize 200,000,000 shares of common stock, par value \$0.0001 per share, and 10,000,000 shares of preferred stock, par value \$0.0001 per share, respectively.

Convertible Preferred Stock

In February and March 2020, the Company issued 21,710,814 shares of Series A convertible preferred stock at \$2.0727 per share for net cash proceeds of \$44.7 million (the "Series A Financing"). In connection with the Series A Financing, the Company issued an additional 301,685 shares of its Series A convertible preferred stock at \$1.65816 per share in February 2020.

In January 2021, the Company issued 19,083,979 shares of Series B convertible preferred stock at \$6.55 per share for net cash proceeds of approximately \$124.7 million.

All shares of convertible preferred stock outstanding at the Company's IPO were converted into shares of the Company's common stock.

Shelf Registration Statement

In April 2022, the Company filed a shelf registration statement on Form S-3 (the "2022 Shelf Registration Statement"), which became effective in May 2022. The 2022 Shelf Registration Statement permits: (i) the offering, issuance and sale by the Company of up to a maximum aggregate offering price of \$300.0 million of common stock, preferred stock, debt securities and warrants in one or more offerings and in any combination; and (ii) the offering, issuance and sale by the Company of up to a maximum aggregate offering price of \$100.0 million of our common stock that may be issued and sold under an "at-the-market" sales agreement (the "ATM Program"). The \$100.0 million of common stock that may be issued and sold under the ATM Program is included in the \$300.0 million of securities that may be issued and sold under the 2022 Shelf Registration Statement. As of December 31, 2022, the Company has not sold any shares of its common stock under the ATM Program.

Shares Subject to Repurchase

Pursuant to the 2018 Plan, the Company has issued shares of restricted common stock to employees, consultants and members of its board of directors. Additionally, certain stock options granted pursuant to the 2018 Plan provide for the right to elect to exercise unvested options early in exchange for restricted shares of common stock. These restricted shares of common stock generally vest over a four-year period and are subject to repurchase by the Company at the original purchase price or, in certain instances the fair market value if such fair market value is lower than the purchase price, in the event the recipient's service is terminated either voluntarily or involuntarily prior to vesting.

A summary of the Company's restricted shares of common stock and unvested stock liability, which is included in accrued expenses and other current liabilities on the Company's balance sheets, is as follows (in thousands, except share data):

	Shares	Liability
Balance at December 31, 2020	646,953	\$ 145
Vested shares	(407,127)	(122)
Balance at December 31, 2021	239,826	23
Vested shares	(192,108)	(14)
Balance at December 31, 2022	<u>47,718</u>	<u>\$ 9</u>

9. Stock-Based Compensation

Equity Incentive Award Plans

In March 2021, the Company's board of directors and stockholders adopted the 2021 Plan, which became effective on March 25, 2021, the date of the underwriting agreement related to the Company's IPO. Upon adoption of the 2021 Plan, the Company restricted future grants from its 2018 Plan.

Under the 2021 Plan, the Company may grant stock options, stock appreciation rights, restricted stock, restricted stock units, performance stock awards, performance cash awards and other forms of stock awards to employees, directors and consultants, including employees and consultants of the Company's affiliates. As of December 31, 2022, the Company had 5,914,999 shares available for grant under the 2021 Plan. In addition, the number of shares of common stock available for issuance under the 2021 Plan will automatically increase on January 1 of each calendar year, starting on January 1, 2022 through January 1, 2031, in an amount equal to 5% of the total number of shares outstanding of the Company's common stock on the last day of the calendar month before the date of each automatic increase, or a lesser number of shares determined by the Company's board of directors. Effective January 1, 2023, the number of shares available for future issuance was increased by 2,797,165 shares so that the total available for future issuance as of January 1, 2023 was 8,712,164 shares.

A summary of the Company's stock option activity for the periods presented was as follows (in thousands, except year, share and per share data):

	Number of Options and Awards Outstanding	Weighted- Average Exercise Price	Weighted- Average Remaining Contractual Term (Years)	Aggregate Intrinsic Value
Outstanding at December 31, 2020	1,601,214	\$ 0.91	9.71	\$ 8,468
Granted	1,439,444	\$ 15.60		
Exercised	(52,974)	\$ 0.65		
Canceled	(313,909)	\$ 3.82		
Outstanding at December 31, 2021	2,673,775	\$ 8.49	9.12	35,343
Granted	3,132,283	\$ 13.50		
Exercised	(226,128)	\$ 1.43		
Canceled/Expired	(183,211)	\$ 9.81		
Outstanding at December 31, 2022	<u>5,396,719</u>	\$ 11.64	8.75	\$ 10,533,451
Vested and expected to vest at December 31, 2022	5,396,719	\$ 11.64	8.75	\$ 10,533,451
Exercisable at December 31, 2022	1,417,736	\$ 7.22	8.07	\$ 8,075,544

The weighted-average grant date fair value per share of options granted was \$8.63 and \$12.39 for the years ended December 31, 2022 and 2021, respectively. The aggregate intrinsic value of options exercised was \$4.0 million and \$0.8 million for the years ended December 31, 2022 and 2021, respectively, and the cash received from options exercised was \$0.3 million and less than \$0.1 million for the years ended December 31, 2022 and 2021.

The weighted-average assumptions used in the Black-Scholes option pricing model to determine the fair value of stock option grants for the periods presented were as follows:

	Year Ended December 31,	
	2022	2021
Fair value of common stock	13.50	15.60
Expected term (years)	6.10	6.07
Expected volatility	70.40%	72.83%
Risk-free interest rate	2.01%	1.04%
Expected dividend yield	0.0%	0.0%

The Company determines the assumptions used in the option pricing model in the following manner:

Fair Value of Common Stock—The grant date fair market value of the shares of common stock underlying stock options is determined by the Company’s board of directors. Following the closing of the Company’s IPO, the fair market value of our common stock is based on its closing price as reported on the date of grant on the primary stock exchange on which the Company’s common stock is traded. Prior to the Company’s IPO, because there was no public market for the Company’s common stock, the board of directors considered, among other things, input from management and valuations of the Company’s stock prepared by unrelated third-party valuation firms.

Expected Term—The expected term of stock options represents the period of time that the awards are expected to be outstanding. Because the Company does not have sufficient historical exercise behavior, it determines the expected term assumption using the simplified method for employees and board members, which calculates the expected term as the average time-to-vesting and the contractual life of the award. The expected term for non-employees is generally the contractual term.

Expected Volatility—Given the Company’s limited historical stock price volatility data, the expected volatility assumption was determined by examining the historical volatilities of a group of industry peers whose share prices are publicly available.

Risk-Free Interest Rate—The risk-free rate assumption is based on the U.S. Treasury yield in effect at the time of the grant with maturities consistent with the expected term of the awards.

Expected Dividend Yield—The expected dividend yield assumption is based on the Company’s history and expectation of dividend payouts. The Company has not paid and does not intend to pay dividends and, therefore, used an expected dividend yield of zero.

2021 Employee Stock Purchase Plan

In March 2021, the Company’s board of directors and stockholders adopted the ESPP, which became effective on March 25, 2021, the date of the underwriting agreement related to the Company’s IPO. The ESPP permits eligible employees who elect to participate in an offering under the ESPP to have up to 15% of their eligible earnings withheld, subject to certain limitations, to purchase shares of common stock pursuant to the ESPP. The price of common stock purchased under the ESPP is equal to 85% of the lower of the fair market value of the common stock at the commencement date of each offering period or the relevant date of purchase.

A total of 600,000 shares of common stock were approved to be initially reserved for issuance under the ESPP. In addition, the number of shares of common stock available for issuance under the ESPP will automatically increase on January 1 of each calendar year, starting on January 1, 2022 through January 1, 2031, in an amount equal to the lesser of (i) 1% of the total number of shares outstanding of the Company’s common stock on the last day of the calendar month before the date of each automatic increase and (ii) 1,200,000 shares; provided that before the date of any such increase, the Company’s board of directors may determine that such increase will be less than the amount set forth in clauses (i) and (ii). Effective January 1, 2023, the number of shares available for issuance

was increased by 559,433 shares so that the total available for future issuance as of January 1, 2023 was 1,669,360 shares.

As of December 31, 2022, the Company had issued 46,890 shares of the Company's common stock under the ESPP and had 1,109,927 shares available for future issuance.

In determining the grant date fair value of shares to be issued under the ESPP, the Company uses the Black-Scholes option pricing model. The Black-Scholes inputs are determined in the same manner as for stock option awards. The weighted average inputs used for the ESPP for the year ended December 31, 2022, were as follows:

	Year Ended December 31,	
	2022	2021
Fair value of common stock	12.51	19.96
Expected term (years)	1.26	1.41
Expected volatility	78.01%	69.26%
Risk-free interest rate	2.78%	0.18%
Expected dividend yield	0.0%	0.0%

Stock-based compensation expense for all equity awards has been reported in the statements of operations and comprehensive loss as follows (in thousands):

	Year Ended December 31,	
	2022	2021
Research and development	\$ 4,827	\$ 1,827
General and administrative	6,098	2,862
Total	<u>\$ 10,925</u>	<u>\$ 4,689</u>

As of December 31, 2022, unrecognized compensation expense related to unvested stock option awards was \$33.2 million, which is expected to be recognized in expense over a weighted-average period of 2.8 years. As of December 31, 2022, unrecognized compensation expense related to ESPP rights was \$0.4 million, which is expected to be recognized over a remaining period of 1.6 years.

10. Income Taxes

The Company is subject to taxation in the United States and various state jurisdictions. All of the Company's tax years are subject to examination by federal and state tax authorities due to the carryforward of unutilized net operating losses and research and development credits. The Company's policy is to recognize interest and penalties related to income tax matters as tax expense. The Company had no accrued interest or penalties related to income tax matters on its balance sheets at December 31, 2022 or 2021, and has not recognized interest or penalties in its statements of operations and comprehensive loss for the years ended December 31, 2022 and 2021, respectively. Further, the Company is not currently under examination by any federal, state or local tax authority.

At December 31, 2022, the Company had federal and state net operating loss ("NOL") carryforwards of \$54.8 million and \$10.6 million, respectively. Federal NOL carryforwards totaling \$0.1 million begin to expire in 2037, unless previously utilized. Federal and state NOL carryforwards of \$54.7 million and \$0.4 million generated after 2017, may be carryforward indefinitely but can only be utilized to offset 80% of future taxable income. State NOL carryforwards totaling \$10.2 million begin to expire in 2037, unless previously utilized. In addition, the Company has federal and state research and development ("R&D") credit carryforwards totaling \$3.1 million and \$1.4 million, respectively. The federal R&D credit carryforwards will begin to expire in 2038 unless previously utilized. The state R&D credit carryforwards do not expire.

Utilization of the Company's NOL and R&D credit carryforwards may be subject to substantial annual limitations in the event a cumulative ownership change has occurred, or that could occur in the future, as required by Section 382 of the Internal Revenue Code of 1986, as amended (the "Code"). In general, an "ownership change," as

defined by Section 382 of the Code, results from a transaction, or series of transactions over a three-year period, resulting in an ownership change of more than 50% of the outstanding common stock of a company by certain stockholders or public groups. Such an ownership change may limit the amount of NOL and R&D credit carryforwards that can be utilized annually to offset future taxable income and tax, respectively. The Company completed a study to assess whether an ownership change had occurred from the Company's formation through December 31, 2021. Based upon the study, the Company determined that it had experienced multiple ownership changes during 2020, causing the annual utilization of the NOL and credit carryforwards to be limited. The Company does not believe any of the NOL and credit carryforwards generated through December 31, 2022 would expire solely as a result of annual limitations on the utilization of those attributes. If ownership changes occur in the future, the amount of remaining tax attribute carryforwards available to offset taxable income and income tax expense in future years may be restricted or eliminated. If eliminated, the related asset would be removed from deferred tax assets with a corresponding reduction in the valuation allowance. Due to the existence of the valuation allowance, limitations created by future ownership changes, if any, will not impact the Company's effective tax rate.

Significant components of the Company's net deferred tax assets at December 31, 2022 and 2021 were as follows (in thousands):

	December 31, 2022	December 31, 2021
Deferred tax assets:		
Net operating losses	\$ 12,240	\$ 9,171
Capitalized research costs	8,396	—
Research and development credits	3,274	1,013
Lease liability	776	763
Stock-based compensation	1,740	532
Other	1,519	515
Total gross deferred tax assets	27,945	11,994
Valuation allowance	(26,777)	(11,235)
Total deferred tax assets	1,168	759
Deferred tax liabilities:		
Right of use asset	(759)	(759)
Other	(409)	—
Total deferred tax liabilities	(1,168)	(759)
Net deferred tax assets	\$ —	\$ —

A reconciliation of the Company's income tax expense (benefit) to the amount computed by applying the federal statutory income tax rate for the periods presented were as follows (in thousands):

	December 31, 2022	December 31, 2021
Expected tax benefit at federal statutory rate	\$ (13,295)	\$ (7,451)
State income taxes, net of federal benefit	(15)	(4)
Debt financing	—	—
Research and development credits	(2,075)	(836)
Stock-based compensation	697	326
Other	(200)	(9)
Change in valuation allowance	14,888	7,974
Provision for income taxes	\$ —	\$ —

The Company recognizes a tax benefit from an uncertain tax position when it is more likely than not that the position will be sustained upon examination by tax authorities. The Company does not expect that there will be a significant change in the unrecognized tax benefits over the next twelve months. Further, due to the existence of the

valuation allowance, future changes in the Company's unrecognized tax benefits will not impact the effective tax rate.

The following table summarizes the changes to the Company's unrecognized tax benefits for the periods presented (in thousands):

	December 31, 2022	December 31, 2021
Balance at beginning of period	\$ 418	\$ 15
Increase related to prior year tax positions	—	1
Increase to current year tax positions	511	402
Balance at end of period	<u>\$ 929</u>	<u>\$ 418</u>

11. Commitments and Contingencies

Contingencies

From time to time, the Company may become subject to claims or suits arising in the ordinary course of business. The Company accrues a liability for such matters when it is probable that the future expenditures will be made and such expenditures can be reasonably estimated. The Company had no such contingent liabilities as of December 31, 2022 or December 31, 2021.

12. License Agreement

In February 2019, the Company entered into a Human Therapeutics Exclusive License Agreement (the "License Agreement") with the Wisconsin Alumni Research Foundation ("WARF"). Under the License Agreement, the Company licensed the exclusive, worldwide, royalty-bearing, sublicensable rights to certain WARF patents and the nonexclusive worldwide rights to certain know-how to develop and commercialize products for the prevention, diagnosis and treatment of disease. As consideration for the license, the Company agreed to pay an upfront fee of \$0.3 million, which the Company immediately expensed as research and development expense in its statements of operations as there was no alternative future use for the license.

For the year ended December 31, 2022, pursuant to the License Agreement, the Company paid \$0.1 million upon the acceptance of an Investigational New Drug Application ("IND") in the U.S. The Company will be required to make further aggregate milestone payments of up to \$17.5 million upon achievement of certain other regulatory and commercial milestones. The Company may also be required to pay royalties based on annual net product sales in the low single digits on its or its sublicensees' net product sales on a country-by-country and product-by-product basis, and is subject to a minimum royalty of \$0.1 million per calendar year upon first commercial product sale. Further, the Company may be required to pay sublicense fees in the mid-single digits percentage for fees, royalties or other payments earned from the granting of sublicenses to the WARF patents and know-how.

The Company is responsible for reimbursing WARF for costs incurred in connection with prosecuting and maintaining patent rights that are specific to the License Agreement. Expenses recognized in connection with legal patent fees under this License Agreement were less than \$0.1 million for the years ended December 31, 2022 and 2021, which were recorded as general and administrative expenses in the statements of operations.

The Company may terminate the License Agreement with 90 days written notice or for certain breaches of the agreement. WARF may terminate the License Agreement with 90 days written notice if first commercial sale does not occur before December 31, 2031. Unless terminated earlier by the parties, the term of the License Agreement will continue until the last licensed patent expires in all countries.

13. Related Party Transactions

Lease Agreement

In February 2021, the Company entered into the Lease with Crossing Holdings, LLC to rent laboratory and office space. In March 2022, the Company entered into the Lease Amendment with Crossing Holdings, LLC amending the Lease for additional space in the same building. The Company's Executive Chairperson, co-founder and member of its board of directors, is the sole member and Manager of Crossing Holdings, LLC.

Expenses recognized by the Company under the Lease and Lease Amendment during the periods presented were as follows (in thousands):

	Year Ended December 31,	
	2022	2021
Research and development	\$ 780	\$ 225
General and administrative	290	88
Total expenses	<u>\$ 1,070</u>	<u>\$ 313</u>

Consulting Agreements

In January 2019, the Company entered into an agreement with the Marlinspike Group, LLC (“Marlinspike Group”) for research support, management, and business consulting services (the “2019 Consulting Agreement”). Further, Marlinspike Group provides the use of approximately 2,120 square feet of its office space in Carlsbad, California to the Company on an as-available basis from time to time pursuant to the agreement. The Company’s Executive Chairperson, co-founder and member of its board of directors is an executive officer of Marlinspike Group.

The term of the 2019 Consulting Agreement was for a one-year period, subject to automatic one-month renewals unless terminated upon 14 days’ written notice. In March 2020, the Consulting Agreement was terminated and replaced with an amended consulting agreement (the “2020 Consulting Agreement”), which provides for the similar services and use of office space for a monthly fee of \$20,000. Pursuant to the terms of the 2020 Consulting Agreement, it shall remain in effect until otherwise terminated. Termination may occur at any time upon mutual agreement or unilaterally upon 30 days’ written notice. If the Company unilaterally terminates the 2020 Consulting Agreement for any reason other than cause, it would be subject to a \$240,000 termination fee. The Company cannot determine when, or if, such a termination will occur and hence has not recorded a liability for the fee.

Expenses recognized by the Company under the 2020 Consulting Agreement during the periods presented were as follows (in thousands):

	Year Ended December 31,	
	2022	2021
General and administrative	240	240
Total expenses	<u>\$ 240</u>	<u>\$ 240</u>

In December 2017, the Company entered into a consulting agreement with Aseem Z. Ansari, Ph.D. Dr. Ansari, a co-founder, provides consulting services and advises on certain research and development activities (the “Research Consulting Agreement”). Pursuant to the Research Consulting Agreement, as amended, Dr. Ansari performs these services for a monthly fee of \$15,000.

Expenses recognized by the Company under the Research Consulting Agreement during the periods presented were as follows (in thousands):

	Year Ended December 31,	
	2022	2021
Research and development	\$ 180	\$ 180
Total expenses	\$ 180	\$ 180

The Company had accrued expenses and other current liabilities of zero and \$15,000 as of December 31, 2022 and 2021, pursuant to its related party consulting agreements.

14. Employee Benefit Plans

The Company maintains a retirement plan, which is qualified under section 401(k) of the Internal Revenue Code of 1986, as amended, for the Company's U.S. employees. The plan allows eligible employees to defer, at the employee's discretion, pretax compensation up to the IRS annual limits. The Company is not required to make matching contributions under the plan; however, in 2022, the Company began making matching contributions. The Company voluntarily contributed \$0.3 million to the plan 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***

As required by Rules 13a-15(b) and 15d-15(b) of the Exchange Act, our management with the participation of our Chief Executive Officer and our Chief Financial Officer, 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 a company that are designed to ensure that information required to be disclosed by a company 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 a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company’s management, including its principal executive and principal financial officer, as appropriate to allow timely decisions regarding required disclosure. Management recognizes that any 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 our 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

Management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Exchange Act Rule 13a-15(f). Our internal control over financial reporting is designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of consolidated financial statements for external purposes in accordance with generally accepted accounting principles. Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Management has assessed the effectiveness of our internal control over financial reporting based on the framework set forth by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) in Internal Control-Integrated Framework (2013 framework). Based on our evaluation, management has concluded that our internal control over financial reporting was effective as of December 31, 2022.

Changes in Internal Control over Financial Reporting

There were no changes in our internal control over financial reporting 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.

None.

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

None.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

Information required by this item and not set forth below will be set forth in the sections headed *Election of Directors* and *Executive Officers* contained in our definitive Proxy Statement for our 2023 annual meeting of stockholders, to be filed with the Securities and Exchange Commission on or before May 1, 2023 (the “Proxy Statement”).

We have adopted a Code of Business Conduct and Ethics that applies to all officers, directors and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or person performing similar functions. A current copy of the Code of Business Conduct and Ethics is available on the Corporate Governance section of our website at www.designtx.com. If we make any substantive amendments to the Code of Business Conduct and Ethics or grants any waiver from a provision of the Code of Business Conduct and Ethics to any executive officer or director that are required to be disclosed pursuant to SEC rules, we will promptly disclose the nature of the amendment or waiver on our website.

Item 11. Executive Compensation.

The information required by this item will be set forth in the Proxy Statement in the section headed *Executive and Director Compensation* contained in the Proxy Statement and is incorporated herein by reference.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters.

Information required by this item will be set forth in the sections headed *Security Ownership of Certain Beneficial Owners and Management* and *Executive and Director Compensation* contained in the Proxy Statement and is incorporated herein by reference.

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

Information required by this item will be set forth in the sections headed *Certain Related-Person Transactions* and *Information Regarding the Board of Directors and Corporate Governance* contained in the Proxy Statement and is incorporated herein by reference.

Item 14. Principal Accounting Fees and Services.

Information required by this item will be set forth in the sections headed *Ratification of Selection of Independent Registered Public Accounting Firm* contained in the Proxy Statement and is incorporated herein by reference.

PART IV

Item 15. Exhibits, Financial Statement Schedules

The following documents are filed as a part of this Annual Report on Form 10-K:

(1) Financial Statements:

Our Financial Statements are listed in “Index to Financial Statements” under Part II, Item 8 of this Annual Report on Form 10-K.

(2) Financial Statement Schedules:

Schedules not listed above have been omitted because the information required to be set forth therein is not applicable or is shown in the financial statements or notes herein.

(3) Exhibits:

The following exhibits, as required by Item 601 of Regulation S-K are attached or incorporated by reference as stated below.

Exhibit Index

<u>Exhibit Number</u>	<u>Description</u>
3.1	Amended and Restated Certificate of Incorporation (incorporated by reference to Exhibit 3.1 to the Registrant’s Current Report on Form 8-K, filed March 30, 2021).
3.2	Amended and Restated Bylaws (incorporated by reference to Exhibit 3.2 to the Registrant’s Current Report on Form 8-K, filed March 30, 2021).
4.1	Form of Common Stock Certificate (incorporated by reference to Exhibit 4.1 to the Registrant’s Registration Statement on Form S-1, as amended, filed March 22, 2021).
4.2	Amended and Restated Investors’ Rights Agreement, by and between the Registrant and certain of its stockholders, dated January 25, 2021 (incorporated by reference to Exhibit 4.2 to the Registrant’s Registration Statement on Form S-1, filed March 5, 2021).
4.3	Description of the Registrant’s Common Stock (incorporated by reference to Exhibit 4.3 to the Registrant’s Annual Report on Form 10-K for the year ended December 31, 2021, filed with the SEC on March 10, 2022).
10.1*	Form of Indemnity Agreement, by and between the Registrant and its directors and officers (incorporated by reference to Exhibit 10.1 to the Registrant’s Registration Statement on Form S-1, filed March 5, 2021).
10.2*	Design Therapeutics, Inc. 2018 Equity Incentive Plan, as amended, and Forms of Option Grant notice, Option Agreement, Notice of Exercise, Early Exercise Stock Purchase Agreement, Restricted Stock Grant Notice and Restricted Stock Award Agreement thereunder (incorporated by reference to Exhibit 10.2 to the Registrant’s Registration Statement on Form S-1, filed March 5, 2021).
10.3*	Design Therapeutics, Inc. 2021 Equity Incentive Plan, and Forms of Option Grant Notice, Option Agreement and Notice of Exercise thereunder (incorporated by reference to Exhibit 10.3 to the Registrant’s Annual Report on Form 10-K for the year ended December 31, 2021, filed with the SEC on March 10, 2022).
10.4*	Design Therapeutics, Inc. 2021 Employee Stock Purchase Plan (incorporated by reference to Exhibit 10.4 to the Registrant’s Registration Statement on Form S-1, as amended, filed March 22, 2021).
10.5*	Employment Agreement, by and between the Registrant and Pratik Shah, Ph.D., dated March 1, 2020 (incorporated by reference to Exhibit 10.5 to the Registrant’s Registration Statement on Form S-1, filed March 5, 2021).
10.6*	Employment Agreement, by and between the Registrant and João Siffert, M.D., dated September 21, 2020 (incorporated by reference to Exhibit 10.6 to the Registrant’s Registration Statement on Form S-1, filed March 5, 2021).

10.7*	<u>Employment Agreement, by and between the Registrant and Sean Jeffries, dated May 21, 2019 (incorporated by reference to Exhibit 10.7 to the Registrant's Registration Statement on Form S-1, filed March 5, 2021).</u>
10.8*	<u>Non-Employee Director Compensation Policy (incorporated by reference to Exhibit 10.8 to the Registrant's Registration Statement on Form S-1, as amended, filed March 22, 2021).</u>
10.9†‡	<u>Human Therapeutics Exclusive License Agreement, by and between the Registrant and Wisconsin Alumni Research Foundation, dated February 20, 2019 (incorporated by reference to Exhibit 10.9 to the Registrant's Registration Statement on Form S-1, filed March 5, 2021).</u>
10.10‡*	<u>Consulting Agreement, by and between the Registrant and Marlinspike Group, LLC, dated March 1, 2020 (incorporated by reference to Exhibit 10.10 to the Registrant's Registration Statement on Form S-1, filed March 5, 2021).</u>
10.11*	<u>Lease, by and between the Registrant and Crossing Holdings, LLC, dated February 2, 2021 (incorporated by reference to Exhibit 10.11 to the Registrant's Registration Statement on Form S-1, as amended, filed March 5, 2021).</u>
10.12*	<u>First Amendment to Lease Agreement, by and between the Registrant and Crossing Holdings, LLC, dated March 18, 2022 (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K, filed March 22, 2022).</u>
10.13*	<u>Consulting Agreement, by and between the Registrant and Aseem Z. Ansari, Ph.D., dated December 27, 2017, as amended (incorporated by reference to Exhibit 10.12 to the Registrant's Registration Statement on Form S-1, as amended, filed March 22, 2021).</u>
23.1	<u>Consent of Independent Registered Public Accounting Firm</u>
24.1	<u>Power of Attorney (see signature page hereto).</u>
31.1	<u>Certification of Principal Executive and 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.</u>
32.1	<u>Certification of Principal Executive and Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.</u>
101.INS	Inline XBRL Instance Document – the instance document does not appear in the Interactive Data File because XBRL tags are embedded within the Inline XBRL document.
101.SCH	Inline XBRL Taxonomy Extension Schema Document
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

* Indicates management contract or compensatory plan.

† Schedules have been omitted pursuant to Item 601(a)(5) of Regulation S-K. The Registrant undertakes to furnish supplemental copies of any of the omitted schedules upon request by the SEC.

‡ Certain portions of this exhibit have been omitted pursuant to Item 601(b)(10) of Regulation S-K.

Item 16. Form 10-K Summary

None.



Executive Officers

João Siffert, M.D. – Chief Executive Officer and a member of the Board of Directors of Design Therapeutics.

Pratik Shah, Ph.D. – Executive Chairperson and a member of the Board of Directors of Design Therapeutics. Chairman of the board of directors for ARS Pharmaceuticals, Inc. President of Marlinspike Group, LLC.

Sean Jeffries, Ph.D. – Chief Operating Officer of Design Therapeutics.

Directors

Arsani William, M.D. – Managing Partner and Chief Investment Officer of Logos Capital.

Deepa Prasad – Executive Director of the Robinson Life Sciences Business and Entrepreneurship Program at University of California, Berkeley.

Heather Berger, Ph.D., - Former Principal at SR One Capital Management, LP.

John Schmid –Former Chief Financial Officer of Auspex Pharmaceuticals, Inc.

Rodney Lappe, Ph.D., - Former Executive Chairman of Mirati Therapeutics, Inc.

Simeon George, M.D. – Chief Executive Officer of SR One Capital Management, LP.

Stella Xu, Ph.D. – Managing Director of Quan Capital.