



2024

ANNUAL REPORT

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

(Mark One)

☒ ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the fiscal year ended December 31, 2024

OR

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

Commission File Number 001-40288

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

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

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

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

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

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

The aggregate market value of the 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 28, 2024, the last business day of the Registrant's most recently completed second quarter, was approximately \$112,536,269.

The number of shares of Registrant's Common Stock outstanding as of March 6, 2025 was 56,762,678.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive proxy statement for its 2025 Annual Meeting of Stockholders, which the registrant intends to file pursuant to Regulation 14A with the Securities and Exchange Commission no later than April 30, 2025, are incorporated by reference into Part III of this Annual Report on Form 10-K.

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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;
- our expectations for resuming clinical development of our program in Friedrich ataxia and announcing data therefrom and the timing thereof;
- the side effect profile observed in nonclinical testing of DT-216P2 being indicative of the side effect profile that may be expected in clinical trials, and in general the ability of DT-216P2 to prevent injection site thrombophlebitis or other limiting side effects;
- the initiation, progress, success, cost and timing of our nonclinical 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 nonclinical 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;
- the effects of macroeconomic factors on our operations;
- our expected use of the net proceeds from our initial public offering; 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 on Form 10-K. 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 two product candidates in clinical development, with all of our other research programs currently in the nonclinical or discovery stage. We have a limited history of conducting clinical trials to test our product candidates in humans.
- Nonclinical and clinical development involves a lengthy and expensive process with uncertain timelines and outcomes, and results of nonclinical 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 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 clinical trials and perform some of our research and nonclinical 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 nonclinical 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's disease (HD), the nucleotide repeat expansions result in the generation of toxic gene products, often associated with pathological nuclear foci and broad splicing disruptions or the expression of mutant proteins that form toxic aggregates. 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 (NHPs), 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[®] small molecule, DT-216, formulated as the prior DT-216 product candidate, was cleared by the U.S. Food and Drug Administration (FDA) to commence Phase 1 clinical trials. In December 2022, we reported positive initial data from the Phase 1 single-ascending dose (SAD) clinical trial and in August 2023, we reported data from the Phase 1 multiple-ascending dose (MAD) clinical trial of the prior DT-216 product candidate. Both studies showed that DT-216 was generally well-tolerated and exhibited the ability to overcome the FXN transcription impairment that causes FA. Data from the Phase 1 MAD clinical trial suggests more sustained exposure is likely needed to achieve a more durable increase in FXN expression, and we observed five cases of injection site thrombophlebitis in the Phase 1 MAD clinical trial. We then shifted focus to developing DT-216 with a potentially improved formulation to enable higher exposure and chronic administration for treatment of FA. These efforts resulted in a new product candidate, DT-216P2, which uses the same drug substance, DT-216. In nonclinical studies, we observed higher and more sustained DT-216 plasma levels after administration of DT-216P2 than was seen in studies with the prior DT-216 product candidate. Additionally, we observed favorable injection site tolerability following multiple intravenous (IV) administrations of DT-216P2. We have initiated a Phase 1 SAD clinical trial of DT-216P2 in normal healthy volunteers in Australia to evaluate single doses using multiple routes of administration, specifically IV infusion and subcutaneous (SC) injection and infusion routes. Results from this Phase 1 SAD clinical trial will inform the design of a clinical trial in FA patients, anticipated to begin in mid-2025. We anticipate providing an update in 2026 on the effect of DT-216P2 on endogenous FXN levels following 12 weeks of dosing.

In December 2022, we nominated our second GeneTAC[®] small molecule, 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. We have completed dosing in a Phase 1 clinical trial in normal healthy volunteers to evaluate the safety of DT-168 and plan to provide results in the first half of 2025. In addition, DT-168 has been evaluated in chronic toxicity studies of up to nine months in duration. We are currently conducting an observational study in FECD to confirm disease characteristics and evaluate deterioration in the context of running a trial and to identify characteristics of FECD patients at risk of more rapid disease progression. We have achieved our enrollment goal for the observational study by recruiting and completing baseline assessments on approximately 250 FECD patients. Based on the baseline characteristics data, we have chosen approximately 100 patients for future follow-up visits. This will inform our clinical development efforts and we believe it could potentially increase the probability of DT-168 programmatic success.

Our third program based on the GeneTAC[®] platform is focused on DM1. 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 in DM1 patients. We plan to continue evaluating the properties of our DM1 GeneTAC[®] molecules in preclinical studies in order to nominate a development candidate in 2025.

Our fourth program based on the GeneTAC[®] platform is focused on HD. We are currently conducting preclinical studies on promising HD GeneTAC[®] candidate molecules. We have observed reduced mutant huntingtin (mtHTT) mRNA and protein and preservation of wild type huntingtin (wtHTT) in HD patient cells after treatment with our HD GeneTAC[®] candidate molecules. In *in vivo* studies in zQ175DN mice, an animal model of HD, we observed a reduction of over 50% in mtHTT mRNA and protein in the brain striatum after eight weeks of systemic administration of our HD GeneTAC[®] candidate molecules. In the same study, wtHTT mRNA and protein levels were shown to be preserved after treatment with our HD GeneTAC[®] candidate molecules. We plan to continue to evaluate these HD candidate molecules in nonclinical studies. The final development candidate will be based on the molecules that perform favorably in relevant studies.

We have continued to make significant progress in advancing our GeneTAC[®] portfolio in preclinical studies to address other 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.

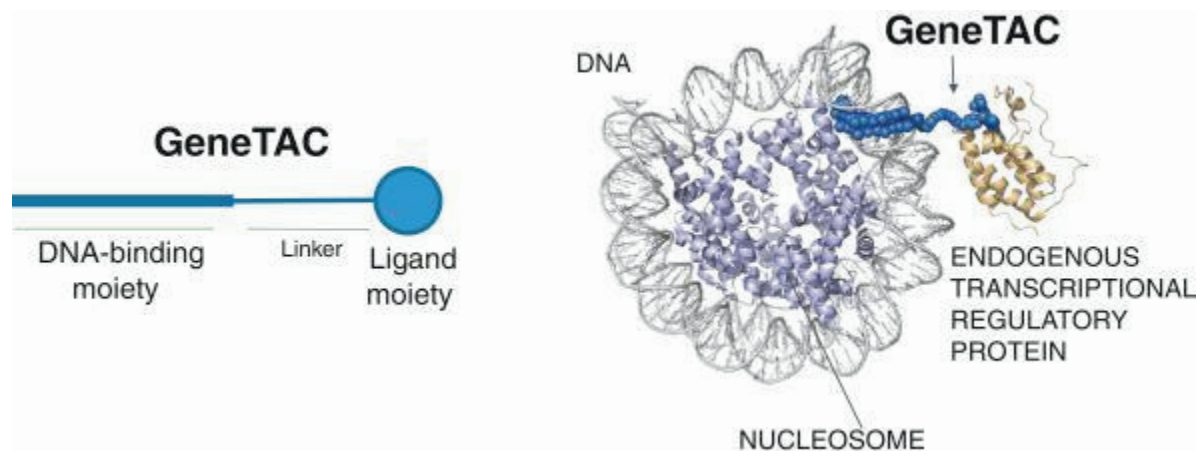
Our GeneTAC[®] Platform

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 guanine-adenine-adenine (GAA) sequence seen in the first intron of the FXN gene seen in FA or the cytosine-thymine-guanine (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. FECD, DM1, HD), 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, DM1 and HD 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 in Figure 1:

Figure 1: GeneTAC® Pipeline

	Friedreich Ataxia	FECD	DM1	Huntington's Disease
Gene	FRAXIN (FXN)	TCF4	DMPK	HUNTINGIN (HTT)
Monogenic disease	GAA repeat expansion leads to reduced transcription	CTG repeat expansion causes nuclear foci & corneal endothelial cell dysfunction	CTG repeat expansion causes nuclear foci & cellular dysfunction	CAG repeat expansion leads to toxic mRNA & protein product
Differentiated profile	New drug product with improved PK & injection site safety in nonclinical studies	Allele-selective reduction of mutant transcript (TCF4) with an eye drop	Allele-selective reduction of mutant DMPK leads to foci resolution & splicing correction	Allele-selective reduction of mutant HTT
Status	DT-216P2: Phase 1 SAD initiated; MAD in pts mid-2025	DT-168: Phase 1 dosing complete; data in 1H 2025	Select DC in 2025	Next step: Select DC

FA Program Overview (DT-216 and DT-216P2)

Our FA program is focused on the development of a potentially disease-modifying treatment. FA is a devastating monogenic, autosomal recessive progressive disease caused by low levels of endogenous FXN due to abnormally expanded 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 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 August 2023, data from the Phase 1 MAD clinical trial with the prior DT-216 product candidate showed that DT-216 was generally well-tolerated and exhibited the ability to overcome the FXN transcription impairment that causes FA. Data from the MAD trial suggests more sustained exposure is likely needed to achieve a more durable increase in FXN expression, and we observed five cases of injection site thrombophlebitis. We then shifted focus to developing DT-216 with a potentially improved formulation to enable higher exposure and chronic administration for treatment of FA. These efforts resulted in a new product candidate, DT-216P2, which uses the same drug substance, DT-216. In nonclinical studies, we observed higher and more sustained DT-216 plasma levels after administration of DT-216P2 than was seen in studies with the prior DT-216 product candidate. Additionally, we observed favorable injection site tolerability following multiple IV administrations of DT-216P2. In October 2023, we withdrew our IND for the prior DT-216 product candidate and plan to submit a new IND with DT-216P2. We have initiated a Phase 1 SAD clinical trial of DT-216P2 in normal healthy volunteers in Australia to evaluate single doses using multiple routes of administration, specifically IV infusion and SC injection and infusion routes. Results from this Phase 1 SAD clinical trial will inform the design of a clinical trial in FA patients, anticipated to begin in mid-2025. We anticipate providing an update in 2026 on the effect of DT-216P2 on endogenous FXN levels following 12 weeks of dosing.

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 eye disease affects millions of people in the United States, with approximately 60-80% of cases caused by a CTG trinucleotide repeat expansion within the 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 support the potential of our FECD GeneTAC[®] small molecules to correct the most common underlying genetic cause of FECD. We have completed dosing in a Phase 1 clinical trial in normal healthy volunteers to evaluate the safety of DT-168 and plan to provide results in the first half of 2025. In addition, DT-168 has been evaluated in chronic toxicity studies of up to nine months in duration. We are currently conducting an observational study in FECD to confirm disease characteristics and evaluate deterioration in the context of running a trial and to identify characteristics of FECD patients at risk of more rapid disease progression. We have achieved our enrollment goal for the observational study by recruiting and completing baseline assessments on approximately 250 FECD patients. Based on the baseline characteristics data, we have chosen approximately 100 patients for future follow-up visits. This will inform our clinical development efforts and we believe it could potentially increase the probability of DT-168 programmatic success.

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 affect more than 70,000 people in the United States. 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 plan to continue evaluating the properties of our DM1 GeneTAC[®] molecules in preclinical studies in order to nominate a development candidate in 2025.

HD Program Overview

Our HD program is focused on the development of a potentially disease-modifying treatment for HD. HD is a dominantly inherited, monogenic neurodegenerative disease characterized by progressive movement, cognitive and psychiatric disorders. Symptoms of HD typically appear between the ages of 30 and 50 and worsen over the next 10 to 25 years, leading to death in approximately 15 years, on average, after the onset of motor signs and symptoms. People with advanced HD need full-time care to help with their day-to-day activities, and they ultimately succumb to pneumonia, heart failure or other complications. HD is caused by a mutation that leads to an increased number of CAG triplet repeats in Exon 1 of the huntingtin (HTT) gene. Expression of mHTT negatively affects many cellular functions, leading to neuronal death and brain atrophy as symptoms manifest. It is estimated that approximately 40,000 people in the United States are affected by HD. Our HD GeneTAC[®] molecules are designed to address the genetic cause of the disease by dialing down the expression of the mHTT gene while preserving the normal HTT gene expression. We have promising HD GeneTAC[®] candidate molecules that were shown to selectively dial down the expression of the mHTT allele in HD patient derived cells as well as a HD mouse model. We plan to continue to evaluate these HD candidate molecules in preclinical studies. The final development candidate selection will be based on the molecules that perform favorably in relevant studies.

Research Program Overview

We are also advancing our GeneTAC[®] product candidate portfolio into development in other diseases. 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 monogenic, autosomal recessive, progressive multi-system disease that affects organ systems highly dependent on mitochondrial function, eventually leading to neurological, cardiac, and metabolic dysfunction. Our FA GeneTAC[®] molecules are specifically designed to restore levels of endogenous 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. In February 2022, the IND for our lead FA GeneTAC[®] small molecule, DT-216, formulated as the prior DT-216 product candidate was cleared by the FDA to commence Phase 1 clinical trials. In December 2022, we reported positive initial data from the Phase 1 SAD clinical trial and in August 2023, we reported data from the Phase 1 MAD clinical trial of the prior DT-216 product candidate. Both studies showed that DT-216 was generally well-tolerated and exhibited the ability to overcome the FXN transcription impairment that causes FA. Data from the Phase 1 MAD clinical trial suggests more sustained exposure is likely needed to achieve a more durable increase in FXN expression, and we observed five cases of injection site thrombophlebitis. Following the Phase 1 MAD clinical trial of the prior DT-216 product candidate, we shifted focus to developing DT-216 with a potentially improved formulation to enable higher exposure and chronic administration for treatment of FA. These efforts resulted in a new product candidate, DT-216P2, which uses the same drug substance, DT-216. In nonclinical studies, we observed higher and more sustained DT-216 plasma levels after administration of DT-216P2 than was seen in studies with the prior DT-216 product candidate. Additionally, we observed favorable injection site tolerability following multiple intravenous administrations of DT-216P2. We have initiated a Phase 1 SAD clinical trial of DT-216P2 in normal healthy volunteers in Australia. We anticipate that we will begin FA patient dosing in mid-2025.
- ***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. We have completed dosing in a Phase 1 clinical trial in normal healthy volunteers to evaluate the safety of DT-168 and plan to provide results in the first half of 2025. In addition, DT-168 has been evaluated in chronic toxicity studies of up to nine months in duration. We are currently conducting an observational study in FECD to confirm disease characteristics and evaluate deterioration in the context of running a trial and to identify characteristics of FECD patients at risk of more rapid disease progression. We have achieved our enrollment goal for the observational study by recruiting and completing baseline assessments on approximately 250 FECD patients. Based on the baseline characteristics data, we have chosen approximately 100 patients for future follow-up visits. This will inform our clinical development efforts and we believe it could potentially increase the probability of DT-168 programmatic success.
- ***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 in DM1 patients. We plan to continue evaluating the properties of our DM1 GeneTAC[®] molecules in preclinical studies in order to nominate a development candidate in 2025.

- ***Advance our HD Program Through Clinical Development to Offer Meaningful Patient Benefit.*** HD is a serious monogenic neurodegenerative disease characterized by progressive movement, cognitive and psychiatric disorders. There are currently no approved therapies that can reverse or slow down the course of HD, as a result, patients only receive medications to manage movement and psychiatric symptoms as their conditions continue to deteriorate, leaving a high unmet medical need and opportunity for new disease-modifying therapies. Our HD GeneTAC[®] molecules are designed to address the root cause of HD by selectively dialing down the expression of the toxic mHTT gene. We have promising HD GeneTAC[®] candidate molecules that were shown to selectively dial down the expression of the mutant HTT allele in HD patient-derived cells as well as a HD mouse model. The final development candidate selection will be based on the molecules that perform favorably in relevant studies.
- ***Leverage our GeneTAC[®] Platform to Expand our Pipeline and Address Additional Diseases with Significant Unmet Medical Need.*** We plan to advance our GeneTAC[®] portfolio to develop additional genomic medicines.
- ***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, President, Chief Executive Officer and 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. 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, Current Treatment Landscape and Our Approach

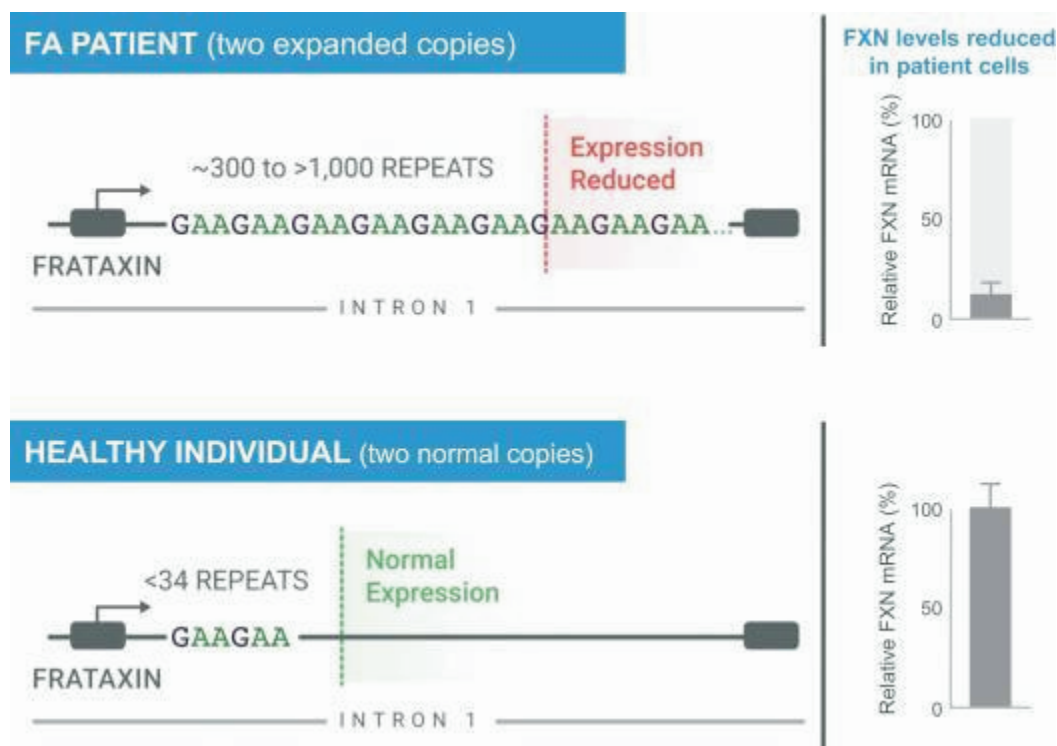
FA is a monogenic, autosomal recessive, progressive multi-system disease that affects organ systems highly dependent on mitochondrial function, eventually leading to neurological, cardiac, and metabolic dysfunction. Clinical manifestations include poor coordination of legs and arms, progressive loss 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.

FA is caused by low levels of endogenous FXN due to abnormally expanded 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 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 (acquired by Biogen) 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 endogenous FXN protein, which is the underlying cause of the disease. There remains a high unmet medical need for disease-modifying therapies, and we believe our FA GeneTAC® molecules present a highly attractive and differentiated profile.

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 endogenous FXN proteins to therapeutic levels.

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-Derived Neurons

Continuous exposure to low doses of DT-216 (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 DT-216 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-derived neurons

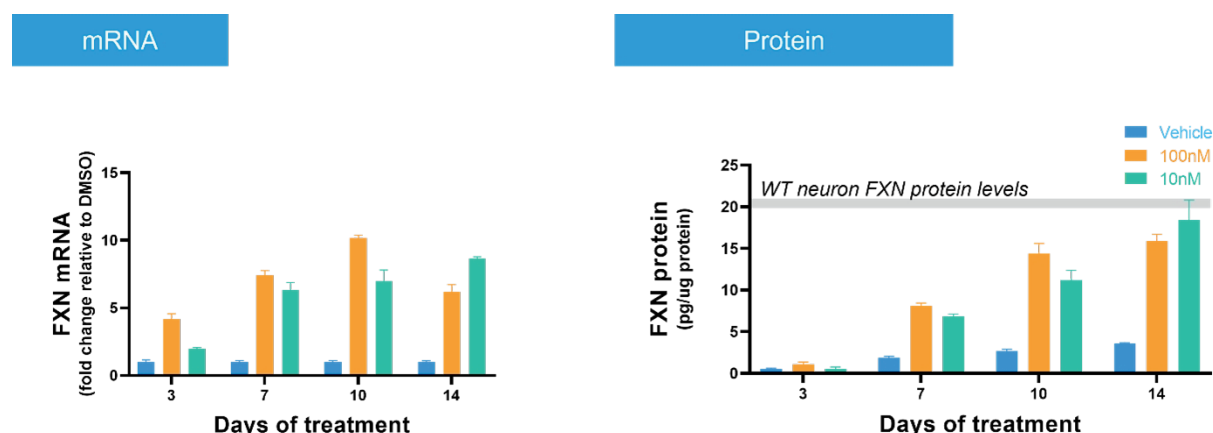


Figure 3. FA patient-derived neurons were incubated with 10 or 100 nM of DT-216 continuously, and cells were harvested for determination of FXN mRNA (left) or protein (right) levels on Days 3, 7, 10, and 14. Data are depicted as Mean \pm SD (n=3/group). Grey horizontal bar (right panel) indicates range 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 GeneTAC[®] molecules.

Background on prior development efforts for DT-216

In preclinical studies for our lead program in FA, at doses that were observed to be well-tolerated in rodents and NHPs, 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. 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 IND for our lead FA GeneTAC[®] small molecule, DT-216, formulated as the prior DT-216 product candidate was cleared by the FDA to

commence Phase 1 clinical trials. In December 2022, we reported positive initial data from the Phase 1 SAD clinical trial showing that DT-216 was generally well-tolerated and exhibited the ability 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 supported the subsequent advancement of DT-216 in the Phase 1 MAD clinical trial of the prior DT-216 product candidate.

In August 2023, we completed the Phase 1 MAD clinical trial of the prior DT-216 product candidate. The Phase 1 MAD clinical trial was a randomized, double-blind, placebo-controlled study designed to evaluate multiple ascending doses of the prior DT-216 product candidate administered intravenously in adult patients with FA. The primary and secondary study objectives were to evaluate safety and tolerability, and pharmacokinetics (PK) of three weekly doses of the prior DT-216 product candidate in FA patients. As an exploratory objective, we also evaluated DT-216 level and FXN in skeletal muscle biopsies obtained at pre-dose baseline and two and seven days after the third weekly dose. Study participants were randomized to receive three weekly intravenous injections across the pooled placebo, 100 mg, 200 mg, and 300 mg cohorts (N=9, 3, 8, 9, respectively). Two subjects did not return for post-dose muscle biopsies due to acute COVID (one in the 200 mg cohort and one in the 300 mg cohort).

In the MAD trial with the prior DT-216 product candidate, we observed that DT-216 levels in plasma and muscle were comparable and the exposures in plasma and muscle were both transient. Following three weekly intravenous administrations of the prior DT-216 product candidate, we observed plasma PK characterized by an extended alpha phase and a rapid decrease in the plasma after only a few hours, reaching ~10nM after seven days. We also observed in the 200 mg and 300 mg cohorts that DT-216 levels in tissue were approximately 8-10 nM two days after the third weekly dose and approximately 1 nM seven days after the third weekly dose.

Figure 4: Prior DT-216 product candidate Phase 1 MAD trial: plasma and muscle DT-216 PK after 3rd dose

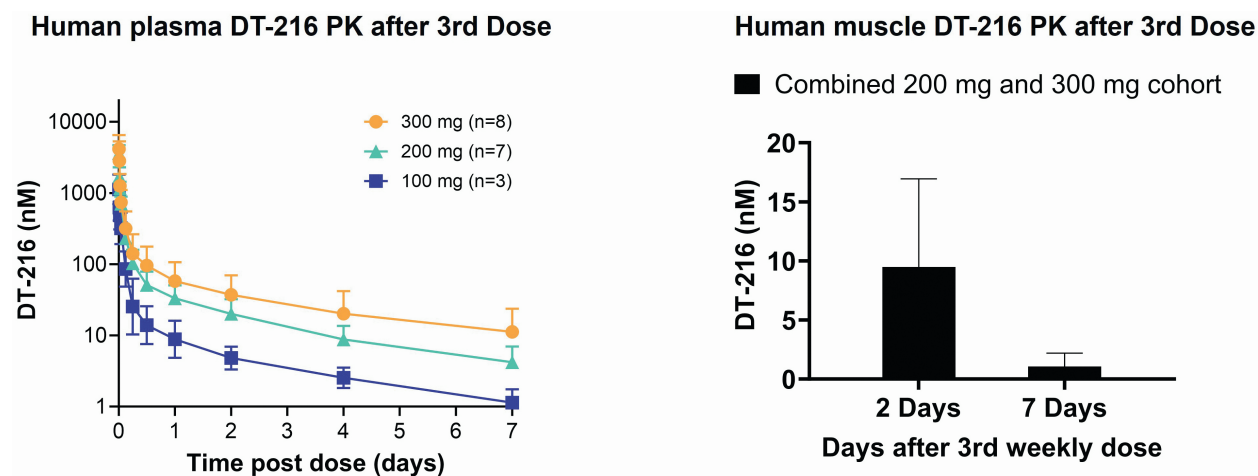


Figure 4. Study participants were randomized to receive three weekly intravenous injections of prior DT-216 product candidate across the 100 mg, 200 mg, and 300 mg cohorts. Plasma and muscle biopsy samples were collected at indicated time points for determination of DT-216 levels by LC-MS/MS. Data are depicted as Mean \pm SD.

DT-216 muscle exposure in FA patients was lower than projected from animal studies but was sufficient to result in significant pharmacodynamic response in skeletal muscle. Exploratory analyses of muscle FXN mRNA levels from the Phase 1 MAD study showed that FA patients in the 300 mg cohort had a significant increase from baseline in FXN mRNA two days after the third weekly dose compared to placebo ($p < 0.05$), with a trend in increased FXN mRNA seven days post dose (Figure 5).

Figure 5: Prior DT-216 product candidate Phase 1 MAD trial: FXN expression in FA Patients

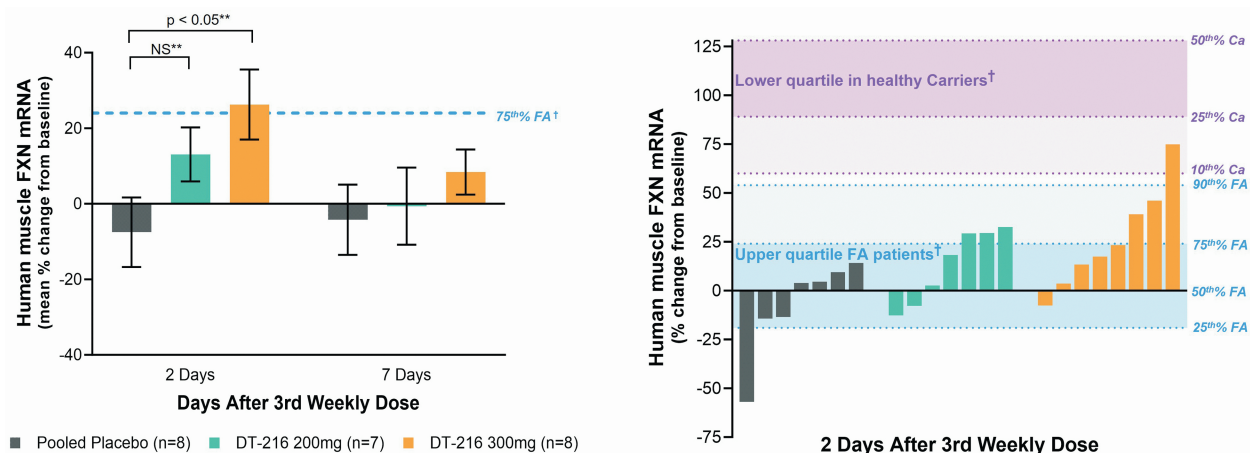


Figure 5. Post-splice FXN mRNA was measured using intron spanning RT-qPCR to detect post-spliced mature mRNA in FA patients two days and seven days after the third weekly dose of prior DT-216 product candidate. Left: Exploratory analyses were conducted using a non-parametric Wilcoxon Rank-Sum model. Data are depicted as Mean \pm SE. NS, not significant. Right: percentiles and quartiles assume individual FA patient baselines in the MAD study are the median FA patient FXN mRNA value from an observational muscle biopsy study.

DT-216 was generally well-tolerated after three intravenous doses of the prior DT-216 product candidate or placebo. There were no serious or severe adverse events and no treatment-related discontinuations. All adverse events were mild or moderate. There were five cases of injection site thrombophlebitis observed in patients who received the prior DT-216 product candidate; one mild in 100 mg cohort; three mild in 200 mg cohort; one moderate in 300 mg cohort, none in placebo group. Nonclinical studies showed that the injection site reactions were attributable to the formulation excipients in the prior DT-216 product candidate.

We believe the results from our Phase 1 MAD trial underscore the promise of DT-216 as a potential disease-modifying treatment for FA. We elected to complete dose escalation in this Phase 1 trial at the 300 mg cohort due to concern for potential worsening of injection site thrombophlebitis at higher doses with multiple administration. We then shifted focus to developing DT-216 with a potentially improved formulation to enable higher exposure and chronic administration for treatment of FA. These efforts resulted in a new product candidate that we call DT-216P2, which uses the same drug substance, DT-216. In nonclinical studies, we observed higher and more sustained plasma PK with DT-216P2 than was seen with the prior DT-216 product candidate. Additionally, we observed favorable injection site tolerability following multiple intravenous administrations of DT-216P2. In October 2023, we withdrew our IND for the prior DT-216 product candidate and plan to submit a new IND with DT-216P2.

New product candidate DT-216P2 nonclinical data

We developed a new product candidate, DT-216P2, using a proprietary and novel excipient. DT-216P2 demonstrated a superior profile than the prior DT-216 product candidate in various nonclinical studies characterized by:

- higher and more sustained plasma PK than was seen with the prior DT-216 product candidate;
- favorable injection site reaction profile;
- suitability for multiple routes of administration and dosing frequency; and
- no change in *in vitro* activity profile.

As shown in Figure 6, when the prior DT-216 product candidate was administered through intravenous injection in NHPs, we observed an extended alpha phase and a rapid decrease of DT-216 concentration in the

plasma. In contrast, DT-216P2 demonstrated 10 to >100-fold higher plasma drug level on Day 1 and Day 7 with 1/10 to 1/4 of the dose compared to the prior DT-216 product candidate. This could be explained by a shorter alpha phase observed in DT-216P2 compared to the prior DT-216 product candidate, as the elimination half-life between the prior and new product candidates are similar.

When DT-216P2 was administered subcutaneously, we also observed a sustained exposure profile, with more than 2-fold and 30-fold increase in exposure at 1/80 and 1/8 the dose level, respectively, on Day 7 compared to the prior DT-216 product candidate administered through intravenous injection. The plasma PK achieved through subcutaneous administration of DT-216P2 is shown to have a blunted C_{max} and lower peak-to-trough fluctuations.

Figure 6: New product candidate DT-216P2 PK in NHPs

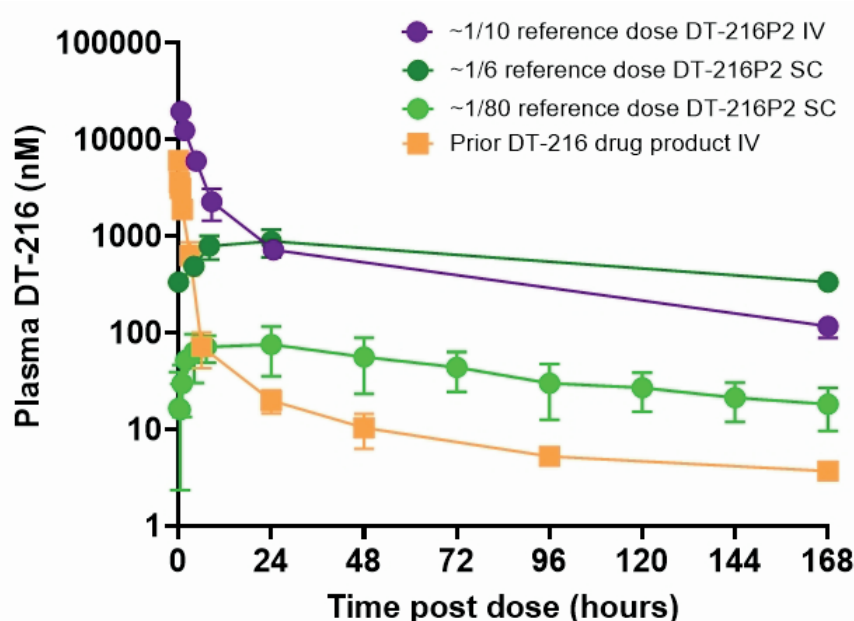


Figure 6. Prior DT-216 product candidate or DT-216P2 was administered once weekly to male cynomolgus monkeys by either IV or SC injection. Plasma and tissues were collected at indicated times after repeat weekly doses for determination of DT-216 levels by LC-MS/MS. Plasma samples were collected at indicated times for determination of DT-216 levels by LC-MS/MS. Data are depicted as Mean \pm SD. Data reflects separate experiments at different times and results were not conducted in a head-to-head study.

In the Phase 1 MAD clinical trial with the prior DT-216 product candidate, we observed that DT-216 concentration in the tissue was comparable with the plasma exposure, as is typical of small molecule drugs. In nonclinical studies, weekly administration of the new product candidate DT-216P2 through intravenous injection was also shown to lead to tissue drug levels that are comparable with plasma drug levels (Figure 7). This suggests that the sustained exposure seen in plasma in NHPs could potentially translate to sustained exposures in tissues in humans.

Figure 7: New product candidate DT-216P2 PK in NHPs compared to the prior DT-216 product candidate PK in humans

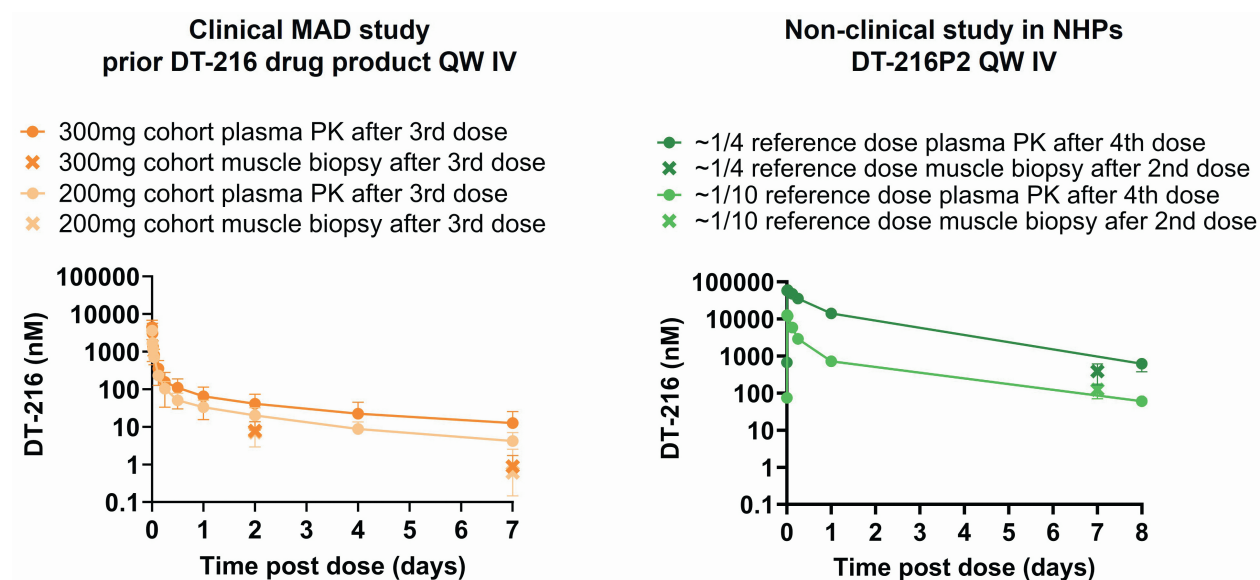


Figure 7. Left: Study participants were randomized to receive three weekly intravenous injections of prior DT-216 product candidate across the 200 mg, and 300 mg cohorts. Plasma and muscle biopsy samples were collected at indicated time points after the third weekly dose for determination of DT-216 levels by LC-MS/MS. Data are depicted as Mean \pm SD. Right: DT-216P2 was administered once weekly by IV injection to male cynomolgus monkeys. Plasma and muscle tissues were collected at indicated times after repeat weekly doses for determination of DT-216 levels by LC-MS/MS. Data are depicted as Mean \pm SD.

This new product candidate DT-216P2 appears compatible with intravenous injections or infusions through either peripheral or central routes of administration, and it was shown to be suitable for subcutaneous route of administration in nonclinical studies. When administered subcutaneously daily or weekly in NHPs, we observed the plasma PK profile shown in Figure 8.

Figure 8: New product candidate DT-216P2 PK administered subcutaneously daily or weekly in NHPs

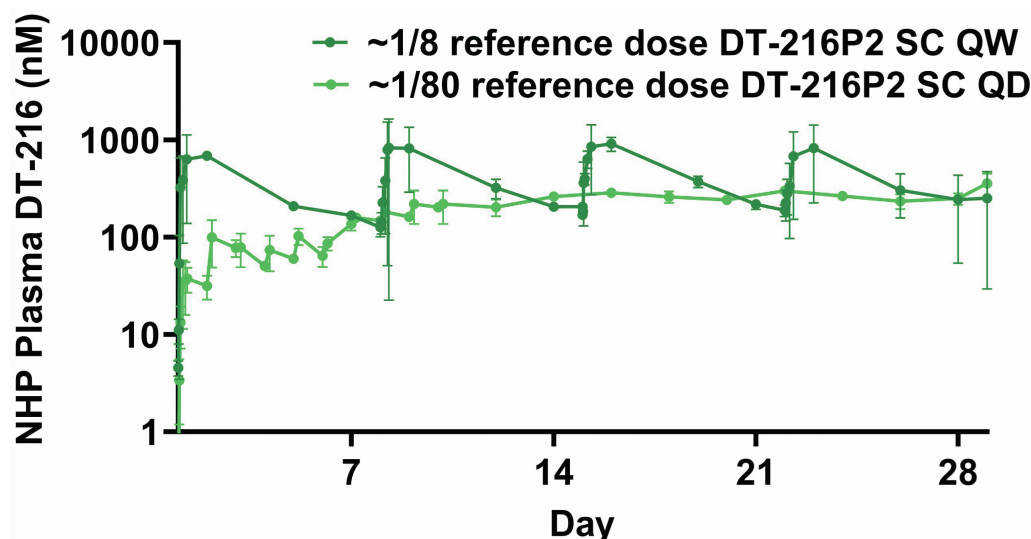
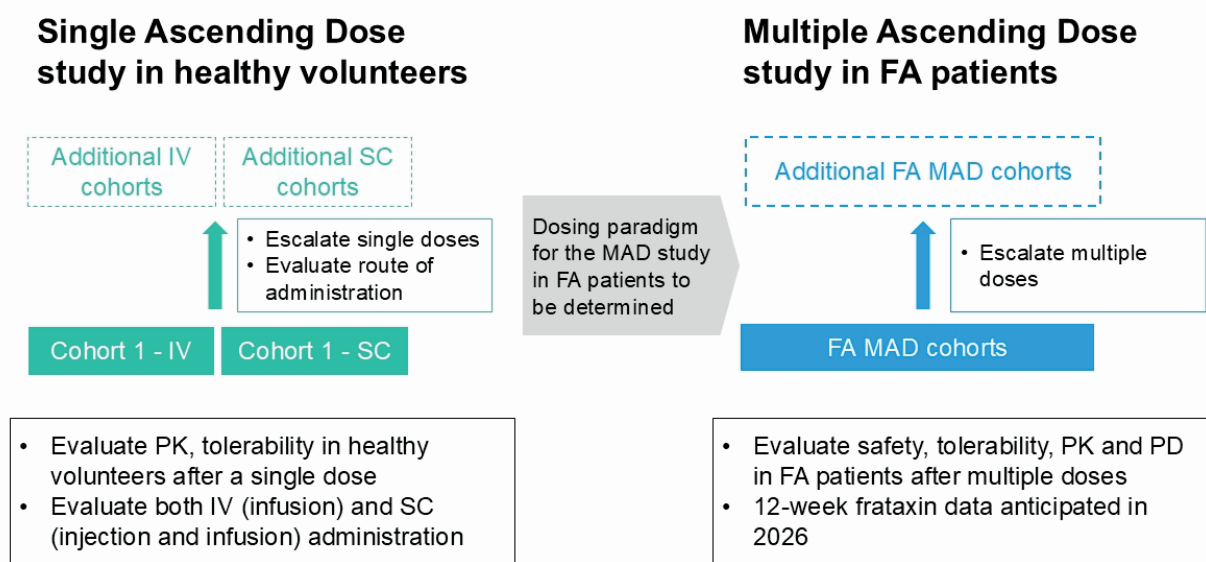


Figure 8. DT-216P2 was administered once weekly or daily to male cynomolgus monkeys by subcutaneous injection. Plasma samples were collected at indicated times for determination of DT-216 levels by LC-MS/MS. Data are depicted as the Mean \pm SD. Data reflects separate experiments at different times and results were not conducted in a head-to-head study.

In animal studies, DT-216P2 has been observed to address the injection site reactions seen with the prior DT-216 product candidate. Repeat administration of DT-216P2 in rats and NHPs was found to be well-tolerated at doses that achieved higher and more durable exposure than the prior DT-216 product candidate. The favorable profile of DT-216P2 has been achieved by using a proprietary and novel excipient in the formulation.

DT-216P2 development efforts and plans

We have initiated a Phase 1 SAD clinical trial of DT-216P2 in normal healthy volunteers in Australia to evaluate single doses using multiple routes of administration, specifically IV infusion and SC injection and infusion routes. Results from this single dose Phase 1 clinical trial will inform the design of a clinical trial in FA patients, anticipated to begin in mid-2025. We anticipate providing an update in 2026 on the effect of DT-216P2 on endogenous FXN levels following 12 weeks of dosing.



Fuchs Endothelial Corneal Dystrophy (FECD)

Disease Overview, Prevalence, Current Treatment Landscape and Our Approach

FECD is characterized by 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 exams. 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, an increase in glare, and can eventually lead to corneal blindness. Other symptoms include pain and grittiness in the eye.

This eye disease affects millions of people worldwide. Approximately 60-80% of FECD cases are caused by 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 FECD.

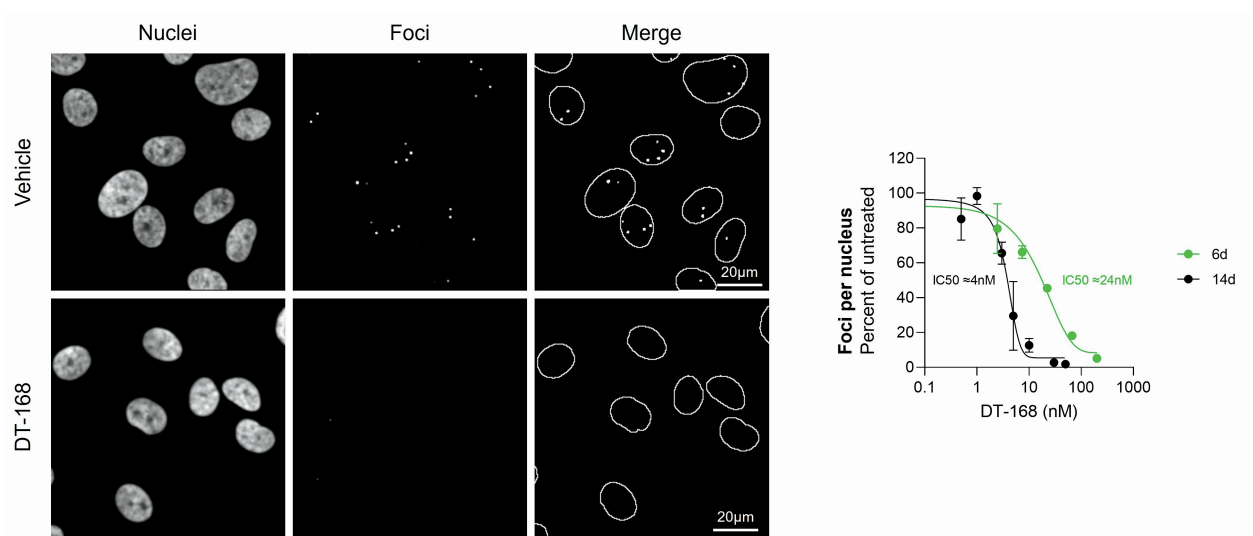
Our FECD program leverages our expertise in designing GeneTAC® small molecules to address the underlying cause of the disease. FECD GeneTAC® molecules we designed have been shown to markedly reduce nuclear foci and improve spliceopathy in FECD CEC cultures derived from the corneal tissue of donors who 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 dial down transcription of the expansion-containing allele while preserving the expression of wild-type TCF4. 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 have completed dosing in a Phase 1 clinical trial in normal healthy volunteers to evaluate the safety of DT-168 and plan to provide results in the first half of 2025. In addition, DT-168 has been evaluated in chronic toxicity studies of up to nine months in duration. We are currently conducting an observational study in FECD to confirm disease characteristics and evaluate deterioration in the context of running a trial and to identify characteristics of FECD patients at risk of more rapid disease progression. We have achieved our enrollment goal for the observational study by recruiting and completing baseline assessments on approximately 250 FECD patients. Based on the baseline characteristics data, we have chosen approximately 100 patients for future follow-up visits. This will inform our clinical development efforts and we believe it could potentially increase the probability of DT-168 programmatic success.

Preclinical Data

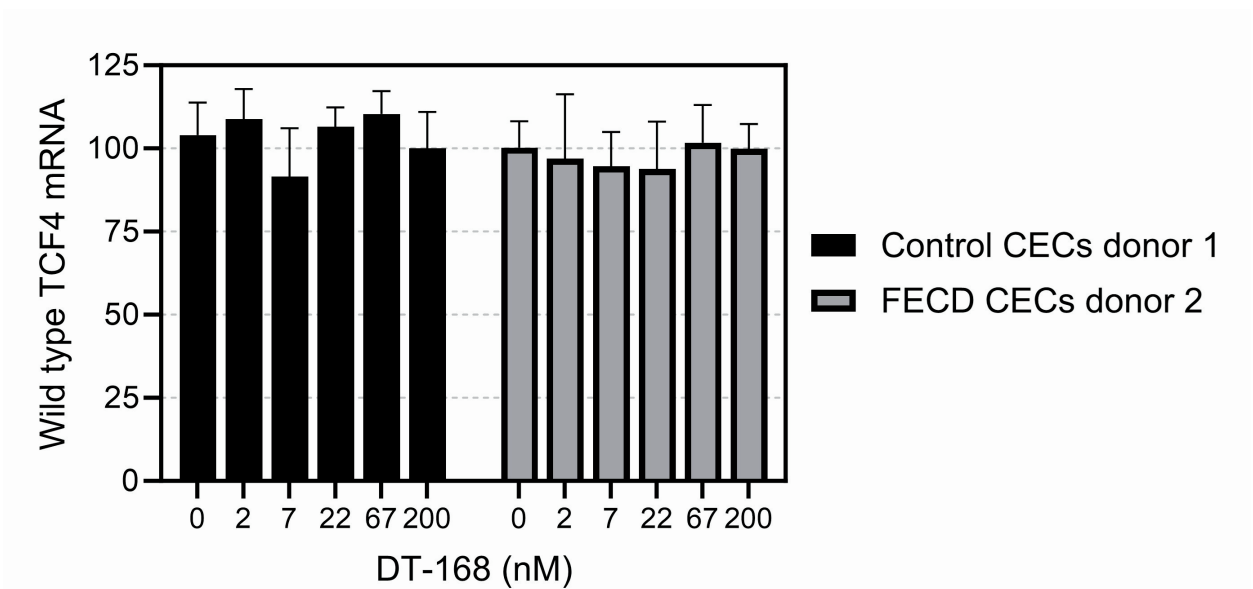
In preclinical studies performed using collected corneal tissue explanted from FECD patients who had undergone keratoplasty, when CECs that contained toxic nuclear TCF4 RNA were treated with DT-168, we observed reduction of pathogenic nuclear foci, and the potency of foci reduction was shown to improve with longer treatment duration. After six days of treatment, DT-168 reduced toxic nuclear foci with a potency of approximately 24 nM, and after 14 days of treatment, DT-168 reduced toxic nuclear foci with a potency of approximately 4 nM (Figure 9).

Figure 9: FECD GeneTAC® molecules reduced pathogenic TCF4 foci in CECs isolated from patients with FECD



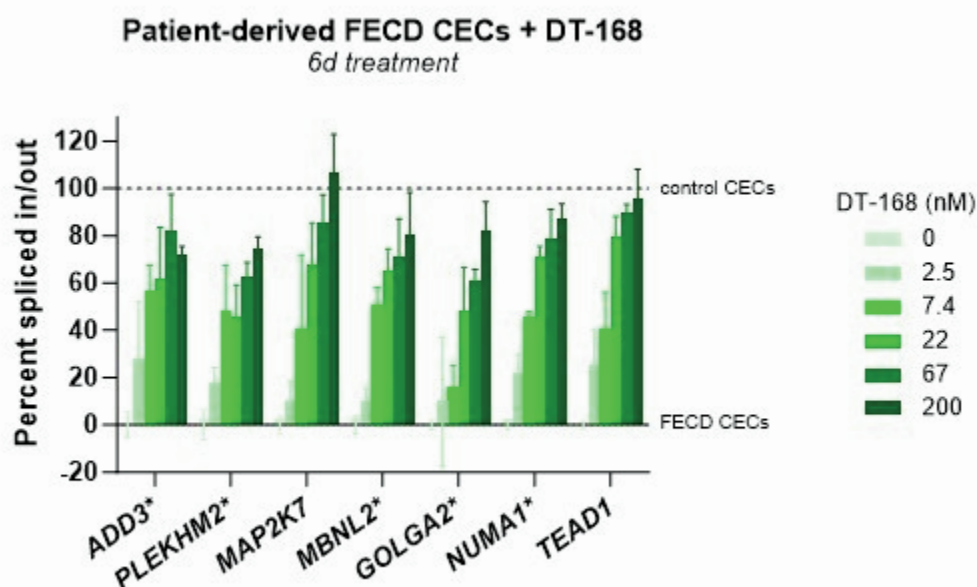
Wild-type TCF4 transcripts are unaffected in primary healthy and FECD CECs following treatment with DT-168. We incubated CECs from a healthy individual and an FECD patient with DT-168 followed by quantification of TCF4 mRNA. As shown in Figure 10, we observed no detectable difference in TCF4 mRNA levels in CECs treated with various concentrations of DT-168 compared with vehicle control. This confirms DT-168 is capable of selectively dialing down transcription of the expansion-containing allele while sparing the wild-type allele.

Figure 10: wild-type TCF4 levels in CECs treated with DT-168



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 11, DT-168 molecules improved spliceopathy in a dose-dependent fashion in FECD patient-derived CECs across genes previously reported as mis-spliced in primary FECD CECs.

Figure 11: DT-168 corrected aberrant splicing events in CECs isolated from patients with FECD



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

These findings support further development of DT-168 as a potential disease-modifying therapy. We have completed dosing in a Phase 1 clinical trial in normal healthy volunteers to evaluate the safety of DT-168 and plan to provide results in the first half of 2025. In addition, DT-168 has been evaluated in chronic toxicity studies of up to nine months in duration. We are currently conducting an observational study in FECD to confirm disease characteristics and evaluate deterioration in the context of running a trial and to identify characteristics of FECD patients at risk of more rapid disease progression. We have achieved our enrollment goal for the observational study by recruiting and completing baseline assessments on approximately 250 FECD patients. Based on the baseline characteristics data, we have chosen approximately 100 patients for future follow-up visits. This will inform our clinical development efforts and we believe it could potentially increase the probability of DT-168 programmatic success.

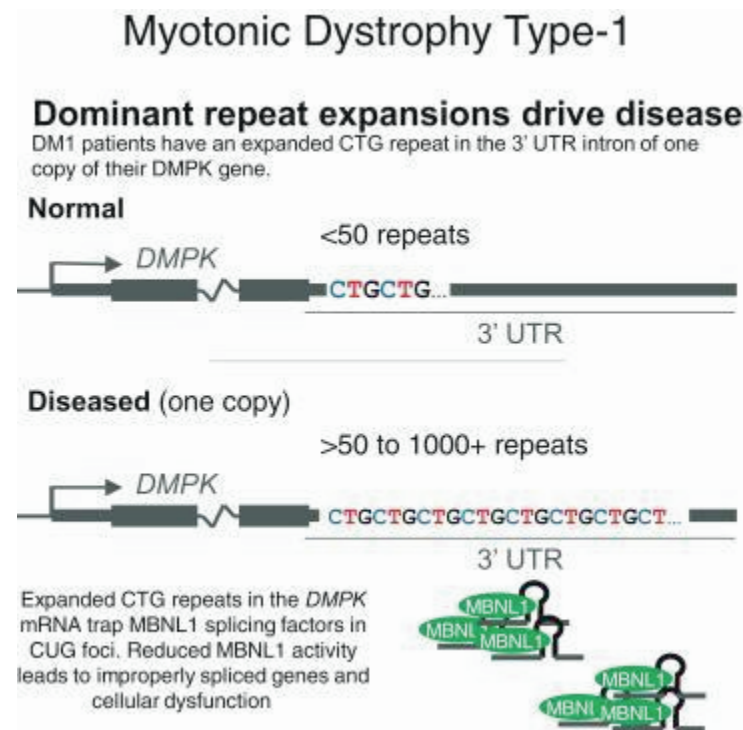
Myotonic Dystrophy Type-1 (DM1)

Disease Overview, Prevalence, Current Treatment Landscape and Our Approach

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 12). The number of repeats ranges from up to approximately 35 in healthy individuals to many thousands in DM1 patients. As the mutant DMPK allele is transcribed, the higher-than-normal number of triplet repeats in terminal end of the mRNA form CUG hairpin loops that are retained in the nucleus. Specifically, the mutant mRNA sequesters a critical CUG-binding protein, muscleblind-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 12: DM1: Genetic basis and clinical presentation



DM1 is estimated to affect more than 70,000 people in the United States. 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. About 25% of people with congenital DM1 die before 18 months of age and 50% die before their mid-30s.

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. Therapeutic modalities currently being evaluated in clinical trials that target reduction in DMPK have observed measurable improvements in one or more clinically assessable endpoints.

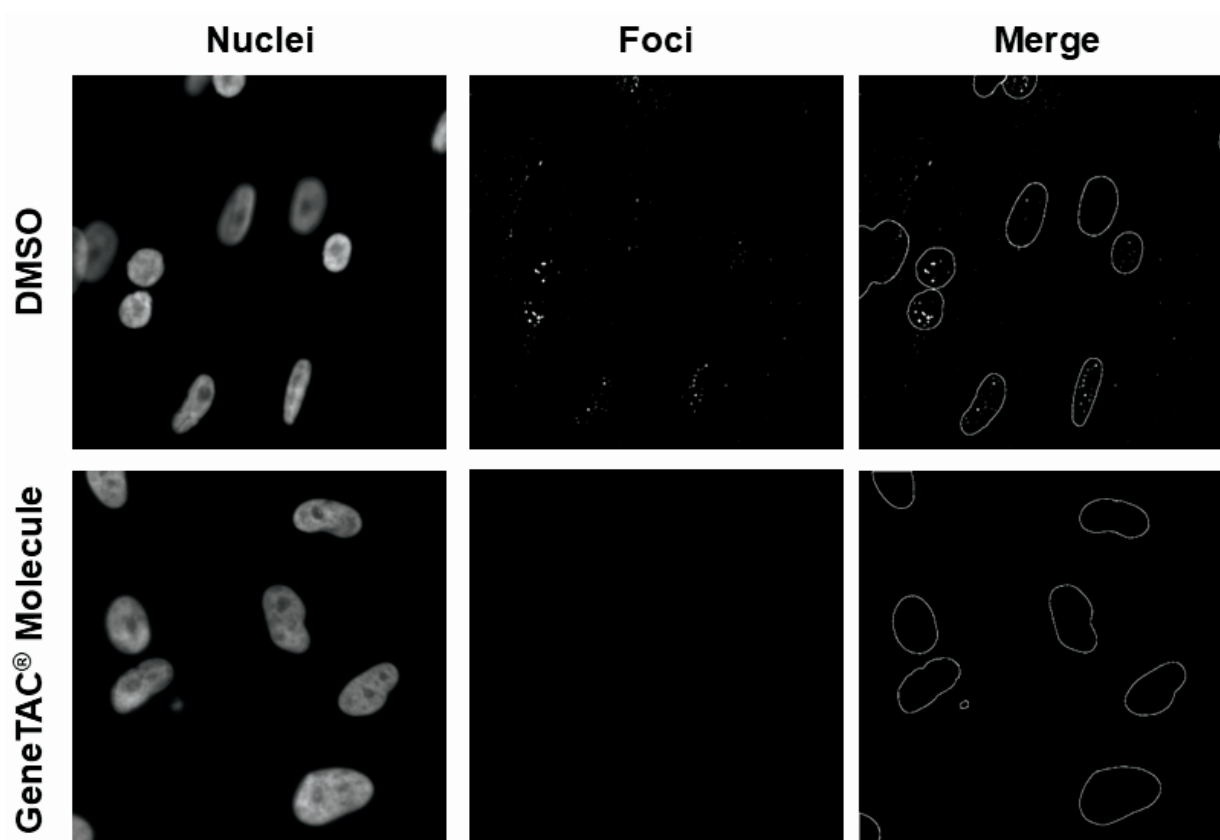
Our DM1 program is based on GeneTAC® small molecule candidates consisting of a DNA-targeting moiety designed to target the CTG repeats in the 3' untranslated region of the DMPK gene, linked to a ligand moiety that is designed to dial down transcription of the mutant expanded CTG repeat without disrupting 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-derived cells. We have observed reduced nuclear foci in DM1 cells derived 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-derived 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 13, we observed a reduction in nuclear foci in DM1 patient-derived 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.

Figure 13: Decrease in nuclear foci in DM1 patient cells exposed to DM1 GeneTAC[®] molecules



In preclinical studies in DM1 patient-derived myotubes, we observed a reduction in the number of observable nuclear foci after exposure to our DM1 GeneTAC[®] molecule. As seen in Figure 14, after exposing DM1 patient-derived myotubes to our DM1 GeneTAC[®] molecule, we observed a dose-dependent decrease of average number foci per nucleus with an IC_{50} of $\sim 6nM$.

Figure 14: Nuclear foci in DM1 patient-derived myotubes treated with DM1 GeneTAC[®] molecule

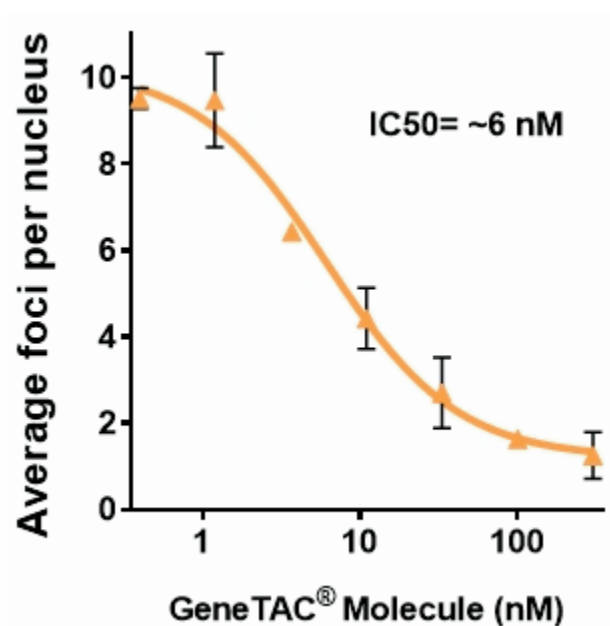
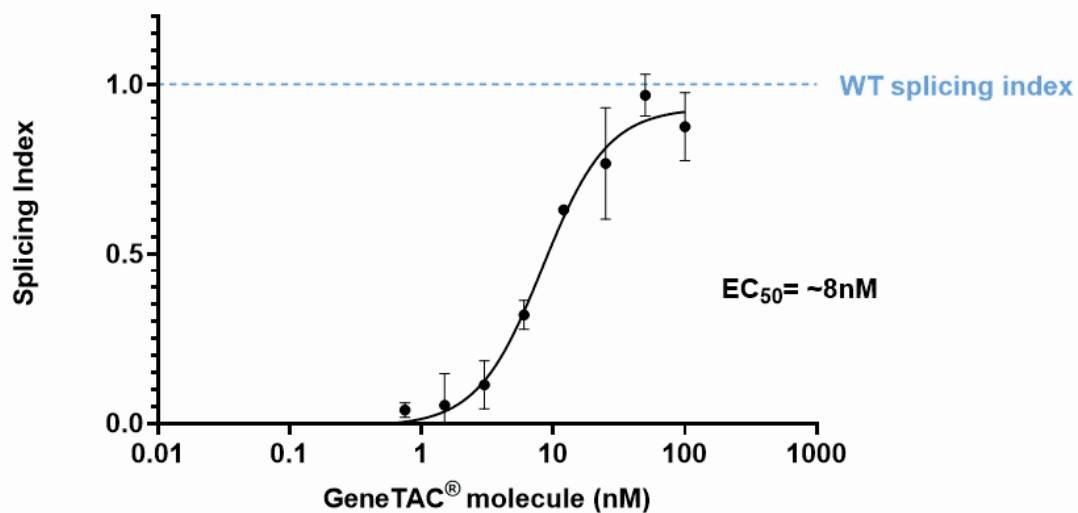


Figure 15: Splicing index correction in DM1 patient-derived myotubes treated with DM1 GeneTAC[®] molecule



DM1 GeneTAC[®] molecules corrected splicing defects in DM1 patient-derived myotubes and restored the splicing index to >90% of that seen in healthy human skeletal myotubes following seven days of treatment (Figure 15). We plan to continue evaluating the properties of our DM1 GeneTAC[®] molecules in both *in vivo* and *in vitro* preclinical studies in order to nominate a development candidate.

Huntington's Disease (HD)

Disease Overview, Prevalence, Current Treatment Landscape and Our Approach

HD is a dominantly-inherited, monogenic neurodegenerative disease characterized by progressive movement, cognitive and psychiatric disorders. Symptoms of HD typically appear between the ages of 30 and 50 and worsen over the next 10 to 25 years, leading to death in approximately 15 years, on average, after the onset of motor signs and symptoms. People with advanced HD need full-time care to help with their day-to-day activities and ultimately succumb to pneumonia, heart failure or other complications. About 10% of HD patients have Juvenile onset HD (JHD), where symptoms manifest before age 20. JHD usually has a more rapid progression rate than adult-onset HD, and death often occurs within 10 years of JHD onset.

HD is caused by an increased number of CAG triplet repeats in Exon 1 of the HTT gene. Expression of this mHTT negatively affects many cellular functions, leading to neuronal death and brain atrophy as symptoms manifest. Longer CAG repeat lengths (>50) are often associated with juvenile or young adult-onset HD and shorter survival after disease onset.

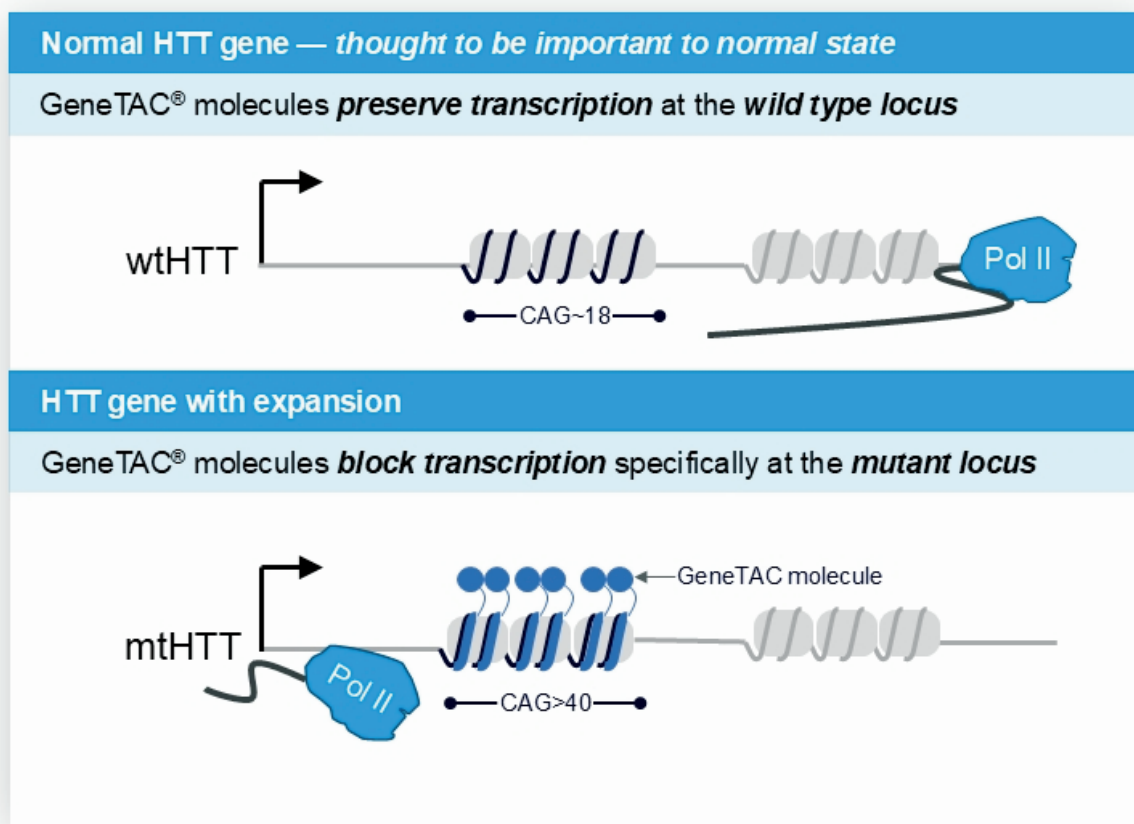
wtHTT is thought to be important for normal neuronal function in the adult central nervous system. It is reported to be involved in axonal transport, protein clearance, synaptic function and cell survival. Increasing lines of evidence also suggest that loss of normal HTT function contributes to the HD pathology. Thus, we believe an allele-selective therapeutic that can dial down mHTT expression and reduce mHTT mRNA and protein while preserving wtHTT expression represents a highly desirable therapeutic profile.

It is estimated that approximately 40,000 people in the United States are affected by HD.

There are currently no approved therapies that can reverse or slow down the course of HD, and as a result, patients only receive medications to manage movement and psychiatric symptoms as their conditions continue to deteriorate, leaving a high unmet medical need and opportunity for new disease-modifying therapies. There are several product candidates currently in preclinical and clinical development designed to address the root cause of HD by lowering the toxic mHTT gene product, with most of them designed to lower both wtHTT and mHTT.

Our HD program is based on GeneTAC[®] molecules consisting of a DNA-targeting moiety designed to target the CAG repeats in the Exon 1 region of the HTT gene, linked to a ligand moiety that is designed to dial down the transcription of the mutant allele without disrupting the normal HTT expression (Figure 16). As a result, the HD GeneTAC[®] molecules are designed to address the root cause of HD by selectively reducing the toxic mHTT gene product, apply to a broad spectrum of HD patients (not restricted by single nucleotide polymorphisms), and benefit from the favorable characteristics of small molecule therapeutics that have the potential to distribute to the whole brain and access many cells.

Figure 16: HD: Our approach



Preclinical Data

We are currently conducting preclinical studies on promising HD GeneTAC[®] candidate molecules in HD patient-derived cells and a zQ175DN mouse model of HD. This is an established HD mouse model that contains a copy of the mutant HTT region of the human gene – the target of our HD GeneTAC[®] molecules. We have observed reduced mtHTT mRNA and protein and preservation of wtHTT in HD patient-derived cells after treatment with our HD GeneTAC[®] candidate molecules. We also observed reduction of mtHTT mRNA and protein in the brain striatum of zQ175DN mice following repeat systemic administration. We believe these data support the potential for our HD GeneTAC[®] molecule candidates to be evaluated in clinical trials as a potential therapy for patients with HD.

We evaluated HD GeneTAC[®] candidate molecules in HD patient-derived cell lines that contained expanded CAG repeats of different lengths in the HTT gene. In HD patient-derived cells with 44 repeats in the mutant allele, we observed selective reduction of mtHTT mRNA of ~75% following exposure to HD GeneTAC[®] candidate molecule 1. In HD patient-derived cells with 180 repeats in the mutant allele, we observed selective reduction of mtHTT mRNA of ~92% following exposure to HD GeneTAC[®] candidate molecule 1 (Figure 17). HD GeneTAC[®] candidate molecule 1 also led to greater reduction of mtHTT protein in HD patient-derived cells with longer repeats (Figure 18). We observed a similar trend in HD patient-derived cells treated with HD GeneTAC[®] candidate molecule 2. These data suggest that our HD GeneTAC[®] molecule candidates are capable of selectively dialing down the expression of mtHTT gene with high efficacy and have the potential to achieve even greater mtHTT inhibition in neurons with longer repeats. This is a favorable therapeutic characteristic as the CAG repeats in the mutant HTT gene are known to go through somatic expansion as disease progresses and longer repeats are associated with juvenile or young adult-onset HD, and our HD GeneTAC[®] candidate molecules can potentially address the disease burden in a broad spectrum of HD patients.

Figure 17: Decreased mtHTT mRNA in HD patient cells exposed to HD GeneTAC® candidate molecules for four days

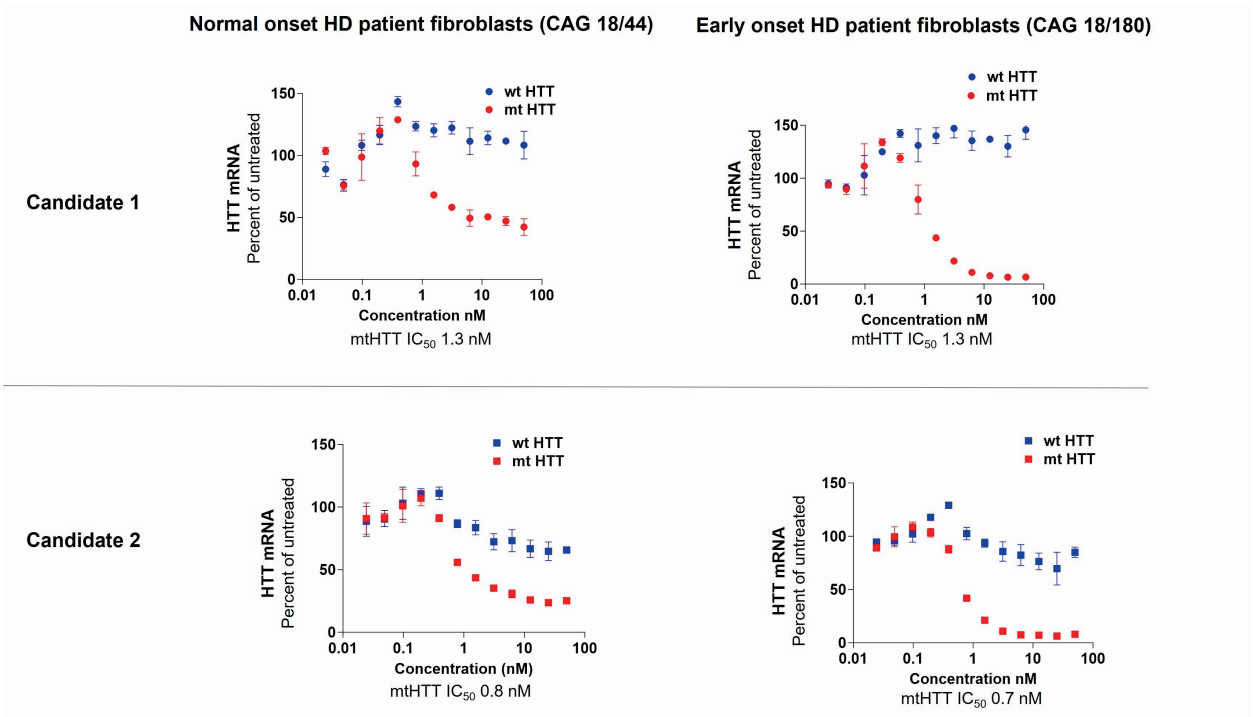
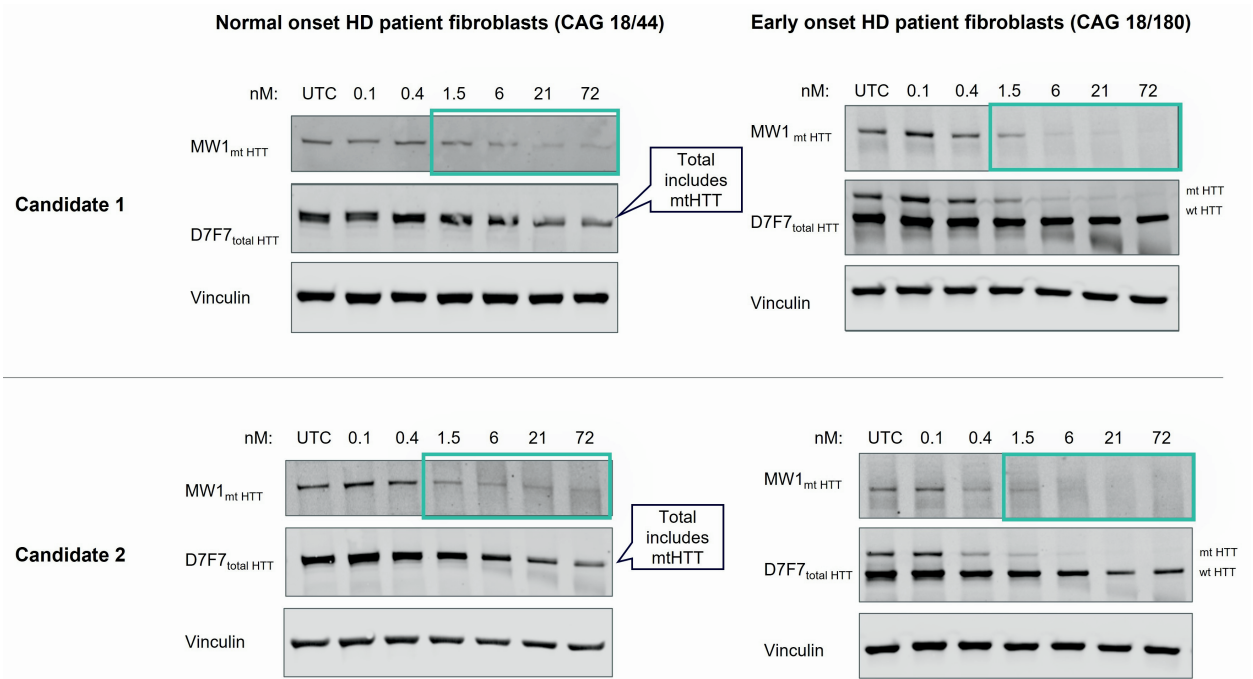
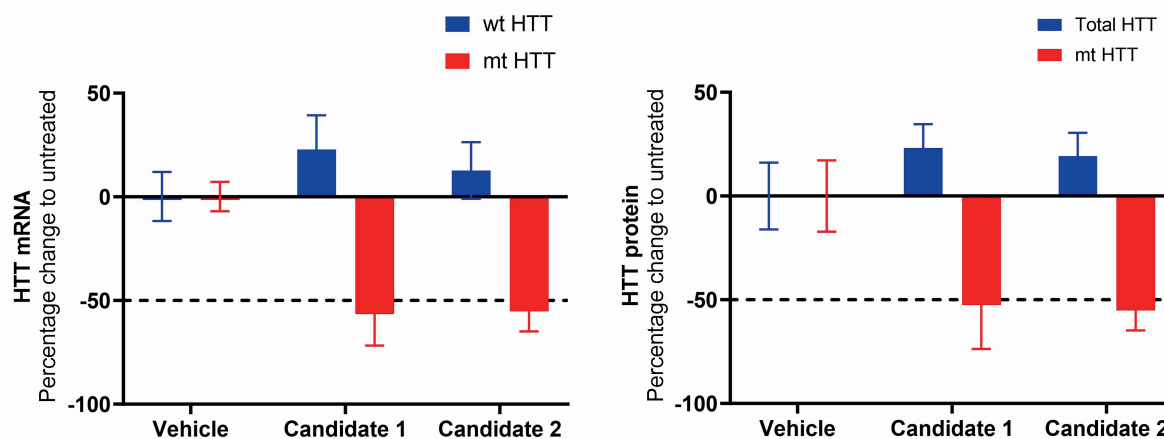


Figure 18: Decreased mtHTT protein in HD patient cells exposed to HD GeneTAC® candidate molecules for seven days



To validate the activity of our HD GeneTAC[®] candidate molecules *in vivo*, we selected the zQ175 neo-deleted knock-in allele (zQ175DN) mouse as a disease model. This strain has a copy of the mutant HTT region of the human gene with a ~190 CAG repeat tract, making it potentially suitable for the evaluation of our HD GeneTAC[®] candidate molecules given their mechanism of action. In *in vivo* studies in zQ175DN mice, we observed a reduction of over 50% in mtHTT mRNA and protein in the brain striatum after eight weeks of systemic administration of our HD GeneTAC[®] candidate molecules. In the same study, wtHTT mRNA and protein levels are preserved after treatment with our HD GeneTAC[®] candidate molecules (Figure 19).

Figure 19: Selective reduction of mtHTT mRNA and protein in zQ175DN mouse brain striatum after treatment with HD GeneTAC[®] candidate molecules for eight weeks



The final development candidate selection will be based on the molecules that perform favorably in relevant studies.

Discovery Programs

We are also advancing our GeneTAC[®] portfolio in other serious diseases. Additionally, our medicinal chemistry experiences with GeneTAC[®] molecules allow us to more rapidly design GeneTAC[®] molecules for additional indications.

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. In February 2023, the FDA approved omaveloxolone, a Nrf2 activator, for the treatment of FA in adults and adolescents aged 16 years and older and omaveloxolone was commercially launched by Reata Pharmaceuticals in June 2023. Reata Pharmaceuticals was acquired by Biogen in September 2023. 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 Astellas Pharma Inc, Capsida Biotherapeutics, Solid Biosciences, 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) Emmeccell 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 (licensed from ActualEyes Inc.), 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) Arrowhead Pharmaceuticals evaluating an RNA interference (RNAi) conjugate, (iii) Arthex Biotech evaluating anti-miRNA oligonucleotides, (iv) Avidity Biosciences evaluating an antibody linked siRNA, (v) Dyne Therapeutics evaluating an antibody linked oligonucleotide, (vi) EditForce evaluating an RNA editing technology, (vii) an AAV-based RNA degrading gene therapy by Enzerna Biosciences, (viii) small molecules interacting with RNA under evaluation by Expansion Therapeutics, (ix) Harmony Biosciences evaluating a histamine 3 receptor for the treatment of excessive daytime sleepiness in DM1, (x) Juvena Therapeutics evaluating JUV-161, a stem cell-secreted protein, (xi) Modalis Therapeutics evaluating MDL-202, a gene therapy candidate, (xii) PepGen evaluating a peptide conjugated antisense oligonucleotide, (xiii) Transition Bio evaluating condensate therapeutics, and (xiv) Vertex Pharmaceuticals evaluating a peptide conjugated oligonucleotide (licensed from Entrada Therapeutics).

Huntington's Disease. We are aware of a number of companies with active clinical-stage HD programs including (i) Alnylam Pharmaceuticals evaluating an RNAi therapeutic, (ii) Annexon Biosciences evaluating a monoclonal antibody, (iii) AskBio evaluating AAV delivered cholesterol 24-hydroxylase gene, (iv) Hoffmann-La Roche AG evaluating Tominersen, an antisense oligonucleotide, (v) Prilenia Therapeutics evaluating a sigma-1 receptor agonist, (vi) PTC Therapeutics evaluating a splicing modifier, (vii) Skyhawk Therapeutics evaluating a splicing modifier, (viii) uniQure evaluating an AAV delivered miRNA, (ix) Vaccinex evaluating a monoclonal antibody, (x) VICO evaluating an antisense oligonucleotide, and (xi) Wave Life Sciences evaluating an antisense oligonucleotide.

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, spinobulbar muscular atrophy and C9orf72-amyotrophic lateral sclerosis/frontotemporal dementia, among others.

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, Rocket Pharmaceuticals, Sangamo Biosciences and Verve Therapeutics.

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, nonclinical 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 FXN, 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. 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 a percentage of any sublicense fees or other payments we receive from a sublicensee of the WARF patents, with the percentage scaling down from a low double-digit percentage to a mid-single digit percentage based on the aggregate of all sublicense fees received by us. 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 \$100,000 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, 2024, the licensed patents include two issued U.S. patents that are projected to expire on or around March 29, 2037 and April 14, 2040. 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.

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 on Form 10-K.

As of December 31, 2024, we own 28 pending U.S. patent applications and 94 pending patent applications in jurisdictions outside of the U.S. (including seven pending Patent Cooperation Treaty applications) which, if issued (or in the case of provisional applications, if issued from future non-provisional applications that we file) have projected expiration dates from 2039 to 2045, not including any patent term adjustments and extensions.

In addition, we acquired an exclusive license from WARF under two issued U.S. patents, three pending U.S. patent applications, two pending applications in Canada, and one pending application each in Australia and Europe, with the issued patents projected to expire on or around March 29, 2037 and April 14, 2040, and the other patents, if issued, having projected expiration dates from 2037 to 2039, not including any patent term adjustments and extensions. These patents and patent applications 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. Under the WARF License Agreement described in more detail above, we are also granted intellectual property rights to know-how that are important to our business.

For our FA program, as of December 31, 2024, we own seven pending U.S. patent applications and 48 pending patent applications in jurisdictions outside of the U.S. directed to compositions of matter and methods for the treatment of FA. Any patents that eventually issue from these patent applications (or in case of provisional applications, if issued from future non-provisional applications that we file) have projected expiration dates from 2039 to 2045. Of the WARF intellectual property described above, one issued U.S. patent, one pending U.S. patent application, and one pending patent application each in Europe and Canada are directed to compounds and methods for modulating FXN 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 one pending patent application each in Australia and Canada directed to methods and compounds for treatment of FA. Any patents that eventually issue from these patent applications are projected to expire on or around October 22, 2039, not including any patent term adjustments and extensions.

For our FECD program, as of December 31, 2024, we own four pending U.S. patent applications, two pending patent applications each in Australia, Canada, China, Europe, Japan, Argentina, and Taiwan, a pending patent application each in Brazil, Hong Kong, Israel, South Korea, and Mexico, and two pending Patent Cooperation Treaty applications directed to compositions of matter and methods for the treatment of FECD. Any patents that eventually issue from these patent applications (or in the case of provisional applications, if issued from future non-provisional applications that we file) have projected expiration dates from 2043 to 2045, not including any patent term adjustments and extensions.

For our DM1 program, as of December 31, 2024, we own three pending U.S. patent applications, two pending patent applications each in Argentina, Taiwan, Australia, Canada, China, Europe, and Japan, one pending patent application each in Brazil, Hong, Kong, Israel, Mexico, and South Korea, and one pending Patent Cooperation Treaty application directed to compositions of matter and methods for the treatment of DM1. Any patents that eventually issue from these patent applications (or in the case of provisional applications, if issued from future non-provisional applications that we file) have projected expiration dates from 2039 to 2044, not including any patent term adjustments and extensions. Of the WARF intellectual property described above, one issued U.S. patent and one pending U.S. patent application are directed to compounds and methods for modulating the expression of the dystrophin myotonia protein kinase (DMPK) gene and methods for the treatment of DM1. This patent is projected to expire on or about April 14, 2040 and any patents that eventually issue from this patent application are projected to expire in 2038, not including any patent term adjustments and extensions.

For our HD program, as of December 31, 2024, we own five pending U.S. patent applications, four pending applications each in Argentina and Taiwan, two pending patent applications each in Australia, Canada, China, Europe, and Japan, one pending patent application each in Brazil, Hong Kong, Israel, Mexico, and South Korea, and three pending Patent Cooperation Treaty applications directed to compositions of matter and methods for the treatment of Huntington's disease. Any patents that issue from these patent applications (or in case of provisional applications, if issued from future non-provisional applications that we file) have projected expiration dates from 2039 to 2044, not including any patent term adjustments or extensions.

As of December 31, 2024, we own 14 pending U.S. patent applications, two pending patent applications in Europe, one pending patent application each in Argentina and Taiwan, and two pending Patent Cooperation Treaty applications directed to our therapeutic programs related to other genetic diseases (including, but not limited to, fragile X syndrome, spinocerebellar ataxias, 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 (or in the case of provisional applications, if issued from future non-provisional applications that we file) have projected expiration dates from 2039 to 2045, not including any patent term adjustments or extensions. Of the WARF intellectual property described above, one issued U.S. patent and one pending U.S. patent application are directed to compounds and methods for 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. This patent is projected to expire on or about April 14, 2040 and any patents that eventually issue from this patent application are projected to expire in 2038, not including any patent term adjustments and extensions.

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. Additionally, 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.

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.

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 Health Insurance Portability and Accountability Act of 1996 (HIPAA), as amended by the Health Information Technology for Economic and Clinical Health Act (HITECH) and their respective implementing regulations, which impose obligations on covered health care providers, health plans, and health care clearinghouses, as well as their business associates that create, receive, maintain or transmit individually identifiable health information for or on behalf of a covered entity and their subcontractors that use, disclose, access, or otherwise process protected health information, with respect to safeguarding the privacy, security and transmission of individually identifiable health information.

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.

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 certain data privacy and security laws, regulations, guidance, and industry standards. In the United States, federal, state, and local governments have enacted numerous data privacy and security laws, including federal health information privacy laws, state data breach notification laws, state health information privacy laws, consumer protection laws (e.g., Section 5 of the Federal Trade Commission Act), and other similar laws (e.g., wiretapping laws). For example, HIPAA, as amended by 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 information, including personal and 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, the California Consumer Privacy Act (CCPA), as amended by the California Privacy Rights Act (CPRA), 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, business representatives, employees, or households. The CCPA requires covered businesses to provide disclosures to consumers about such business’ data collection, use and sharing practices, and provide such consumers ways to opt-out of certain sales or transfers of personal information. The CCPA provides for fines for violations, as well as a private right of action for certain data breaches. Other states have also enacted data privacy laws, including Virginia and Colorado, and similar laws are being considered in several other states, as well as at the federal and local levels. 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, should we become subject to them in the future.

We also are or may become subject to applicable privacy laws outside of the U.S. For example, if we conduct EU-based clinical trials, we may become subject to Regulation (EU) 2016/679, the General Data Protection Regulation and/or the United Kingdom's GDPR (UK GDPR) (collectively, GDPR) in relation to our collection, control, processing and other use of personal data of European Economic Area (EEA) or UK-based data subjects (i.e. data relating to an identifiable living individual). We may in the future process personal data in relation to participants in clinical trials in the European Economic Area (EEA), including health and medical data. 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. Certain jurisdictions have enacted laws requiring data to be localized or limiting the transfer of personal data to other countries. 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 EEA standard contractual clauses and the EU-U.S. Data Privacy Framework and UK extension thereto (which allows for transfers to relevant organizations based in the United States who self-certify compliance and participate in the Framework), 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, which has its own set of stringent privacy and data protection laws and regulations. Under the GDPR, companies may face temporary or definitive bans on data processing and other corrective actions; fines up to 20 million Euros under the EU GDPR / 17.5 million pounds sterling under the UK GDPR, or 4% of the annual global revenue, whichever is greater in either case; 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. 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.

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 pharmacoeconomic 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. The ACA, among other things, increased the minimum level of Medicaid rebates payable by manufacturers of brand name drugs; required collection of rebates for drugs paid by Medicaid managed care organizations; required manufacturers to participate in a coverage gap discount program, under which they must agree to offer point-of-sale discounts (increased to 70 percent, effective as of January 1, 2019) off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D; imposed a non-deductible annual fee on pharmaceutical manufacturers or importers who sell certain "branded prescription drugs" to specified federal government programs, implemented a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted, or injected; expanded the types of entities eligible for the 340B drug discount program; expanded eligibility criteria for Medicaid programs; created a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research; and established a Center for Medicare Innovation at the Centers for Medicare & Medicaid Services (CMS) to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending.

There have been executive judicial and Congressional challenges and amendments to certain aspects of the ACA. For example, on August 16, 2022, the Inflation Reduction Act of 2022, or IRA, was signed 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 current 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 2032, unless additional Congressional action is taken. 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, the IRA, among other things, (i) directs HHS to negotiate the price of certain high-expenditure, single-source drugs and biologics that have been on the market for at least 7 years covered under Medicare (the Medicare Drug Price Negotiation Program), 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 began to take effect progressively starting in fiscal year 2023. On August 15, 2024, HHS announced the agreed-upon price of the first ten drugs that were subject to price negotiations, although the Medicare Drug Price Negotiation Program is currently subject to legal challenges. On January 17, 2025, HHS selected fifteen additional products covered under Part D for price negotiation in 2025. Each year thereafter more Part B and Part D products will become subject to the Medicare Drug Price Negotiation Program. Further, on December 7, 2023, an initiative to control the price of prescription drugs through the use of march-in rights under the Bayh-Dole Act was announced. On December 8, 2023, the National Institute of Standards and Technology published for comment a Draft Interagency Guidance Framework for Considering the Exercise of March-In Rights which for the first time includes the price of a product as one factor an agency can use when deciding to exercise march-in rights. While march-in rights have not previously been exercised, it is uncertain if that will continue under the new framework. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control costs of 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.

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, 2024, we had 54 employees, all of whom were full-time, and 19 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 122 full-time equivalents as of December 31, 2024.

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 nonclinical studies for our lead program in FA and our other development programs, early clinical development for our FA and FECD programs, establishing and enhancing our intellectual property portfolio, and providing general and administrative support for these operations. As a result, none of our product candidates 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 \$49.6 million and \$66.9 million for the years ended December 31, 2024 and 2023, 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 nonclinical 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 nonclinical 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, 2024, we had \$245.5 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, nonclinical 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, European Medicines Agency (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 our current and 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; 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. 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 (such as the geopolitical tensions between the U.S. and China, the ongoing Russia/Ukraine conflict and the Israel-Hamas war), inflation, tariffs, bank failures, global supply chain and labor shortage challenges, and the effects of a health epidemic or pandemic. 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. 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.

Our financial condition could be adversely affected if the financial institutions in which we hold our cash fail.

We maintain cash deposits in Federal Deposit Insurance Corporation (FDIC) insured banks. The bank deposit balances may exceed the FDIC insurance limits, and, currently, we hold our cash in a limited number of accounts. Our access to these balances could be impacted if one or more of the financial institutions in which we deposit monies fails or is subject to other adverse conditions in the financial or credit markets. For example, multiple banks failed and were taken into receivership by the FDIC in the first half of 2023. Our access to cash may be adversely affected in the future by actual or anticipated bank failures.

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

We are early in our development efforts and we have only two product candidates in clinical development, with all of our other research programs currently in the nonclinical 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 nonclinical studies. Our lead FA GeneTAC® small molecule, DT-216, formulated as the prior DT-216 product candidate, entered into a Phase 1 SAD clinical trial in March 2022, the first clinical trial for one of our product candidates and we completed the Phase 1 MAD clinical trial of the prior DT-216 product candidate in August 2023. We withdrew our IND for the prior DT-216 product candidate in October 2023, and have initiated a Phase 1 SAD clinical trial in normal healthy volunteers in Australia to evaluate single doses using multiple routes of administration of DT-216P2, which uses the same drug substance, DT-216. We have also completed dosing in a Phase 1 clinical trial in normal healthy volunteers for DT-168, our FECD GeneTAC® product candidate. As a result, we have limited infrastructure, experience conducting clinical trials as a company and regulatory interactions, and cannot be certain that our 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 product candidates, our ability to eventually generate significant revenues from product sales will depend on a number of factors, including:

- completion of nonclinical 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, DM1 and HD 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.

Nonclinical and clinical development involves a lengthy and expensive process with uncertain timelines and outcomes, and results of nonclinical 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 having promising results in earlier nonclinical studies or clinical trials. These setbacks have been caused by, among other things, nonclinical findings emerging while clinical trials were underway and safety or efficacy observations made in nonclinical studies or clinical trials, including previously unreported adverse events. Although we have initiated clinical trials of DT-216P2, conducted clinical trials of the prior DT-216 product candidate and nonclinical studies of the prior DT-216 product candidate and DT-216P2 for the treatment of patients with FA, completed dosing in a Phase 1 clinical trial of DT-168 in normal healthy volunteers and conducted certain nonclinical studies of DT-168 and certain nonclinical studies of other potential product candidates targeting expansion repeat driven diseases, we do not know whether DT-216P2 or DT-168 or other potential product candidates targeting expansion repeat driven diseases will perform in ongoing or future clinical trials as they have performed in prior studies. Furthermore, for some indications that we are pursuing, such as FECD caused by a nucleotide repeat expansion mutation in the TCF4 gene, there are no animal models of the human disease and therefore our ability to predict human disease outcomes may be reduced.

The results of nonclinical and early clinical trials of our product candidates may not be predictive of the results of later-stage clinical trials. Adverse safety or efficacy observations in nonclinical studies or clinical trials may result in delays in timelines of our programs before or after clinical trials have commenced. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy traits despite having progressed through nonclinical 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.

While we have conducted nonclinical studies of the prior DT-216 product candidate for the treatment of patients with FA, released initial clinical data from our Phase 1 SAD clinical trial in December 2022 and released initial results from the Phase 1 MAD clinical trial of the prior DT-216 product candidate in August 2023 with results showing that DT-216 was generally well-tolerated and exhibited the ability to overcome the FXN transcription impairment that causes FA, previously reported results from the Phase 1 SAD clinical trial showed that three patients on the prior DT-216 product candidate had injection site thrombophlebitis that were mild or moderate and resolved without treatment. DT-216 was generally well-tolerated in the Phase 1 MAD clinical trial. However, self-

limited injection site thrombophlebitis was observed in five patients across all three dose levels (100 mg, 200 mg and 300 mg), whereas injection site thrombophlebitis was only observed at higher doses (the 400 mg and 600 mg cohorts) in the Phase 1 SAD clinical trial. Nonclinical studies showed that the injection site reactions were attributable to the formulation excipients in the prior DT-216 product candidate formulation, and that improving the formulation composition could enable higher doses and chronic administration. We have since shown that a potentially improved formulation using a novel and proprietary excipient with DT-216P2 had favorable injection site tolerability following multiple intravenous administrations and enabled dosing to increase tissue exposure. Given the injection site thrombophlebitis observed in the Phase 1 MAD clinical trial and concern for potential worsening of injection site thrombophlebitis at higher doses with multiple administration, and the initial results from animal studies using a novel and proprietary excipient in DT-216P2, instead of advancing the prior DT-216 product candidate through to Phase 2 in the second half of 2023 as originally planned, we decided to pursue development of DT-216P2 to better support the future clinical development and regulatory pathway for the drug substance DT-216. We withdrew our IND for the prior DT-216 product candidate in October 2023. We have initiated a Phase 1 SAD clinical trial of DT-216P2 in normal healthy volunteers in Australia to evaluate single doses using multiple routes of administration, specifically IV infusion and SC injection and infusion routes. Results from this Phase 1 SAD clinical trial will inform the design of a clinical trial in FA patients, anticipated to begin in mid-2025. We anticipate providing an update in 2026 on the effect of DT-216P2 on endogenous FXN levels following 12 weeks of dosing. However, there can be no assurance that we will be able to successfully develop DT-216P2 with improved injection site tolerability and the absence of other unacceptable side effects on the timeframe we expect, or at all, or that we will be able to achieve our anticipated timeline for resumed Phase 1 clinical development and data.

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 nonclinical 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 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.

Additionally, the policies of the FDA and other regulatory authorities may change and additional government regulations may be enacted that could prevent, limit, or delay regulatory approval of our product candidates. For example, the U.S. Supreme Court's June 2024 decision in *Loper Bright Enterprises v. Raimondo* overturned the longstanding Chevron doctrine, under which courts were required to give deference to regulatory agencies' reasonable interpretations of ambiguous federal statutes. The *Loper* decision could result in additional legal challenges to regulations and decisions issued by federal agencies, including the FDA, on which we rely. Any such

legal challenges, if successful, could have a material impact on our business. Additionally, the *Loper* decision may result in increased regulatory uncertainty, inconsistent judicial interpretations, and other impacts to the agency rulemaking process, any of which could adversely impact our business and operations. We cannot predict the likelihood, nature, or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are unable to maintain regulatory compliance, we may be subject to enforcement action and our business, results of operations, and financial condition could be adversely affected.

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 initiating or completing our 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 GeneTAC® 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 GeneTAC® platform technologies in clinical trials or in obtaining marketing approval thereafter, and use of our GeneTAC® 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 clinical trials or commercializing any products on a timely or profitable basis, if at all. Further, because all of our product candidates and development programs are based on the same GeneTAC® platform technologies, adverse developments with respect to one of our programs may have a significant adverse impact on the actual or perceived likelihood of success and value of our other programs.

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 GeneTAC® platform 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 clinical trials, our clinical development activities could be delayed or otherwise adversely affected.

We may not be able to continue our ongoing clinical trials 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 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 may 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, the FDA approved omaveloxolone for the treatment of FA in adults and adolescents aged 16 years and older in February 2023, and omaveloxolone was commercially launched in June 2023. The commercial availability 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-216P2 or may choose not to do so due to the availability of an approved product. Furthermore, patients enrolled in our clinical trials may receive 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 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, withholding and 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, 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 nonclinical 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 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 clinical trials or nonclinical studies 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 Phase 1 SAD clinical trial for the prior DT-216 product candidate, the first clinical trial for one of our product candidates. Initial safety results from Cohorts 1-5 showed that DT-216 was generally well-tolerated after a single dose of the prior DT-216 product candidate, but three patients on the prior DT-216 product candidate had injection site thrombophlebitis that were mild or moderate and resolved without treatment. DT-216 was generally well-tolerated in the subsequent Phase 1 MAD clinical trial. However, self-limited injection site thrombophlebitis was observed in five patients across all three dose levels (100 mg, 200 mg and 300 mg), whereas injection site thrombophlebitis was only observed at higher doses (the 400 mg and 600 mg cohorts) in the Phase 1 SAD clinical trial. Nonclinical studies showed that the injection site reactions were attributable to the formulation excipients in the prior DT-216 product candidate formulation, and that improving the formulation composition could enable higher doses and chronic administration.

We have since shown that a potentially improved formulation using a novel and proprietary excipient with DT-216P2 had favorable injection site tolerability following multiple intravenous administrations and enabled dosing to increase tissue exposure. Given the injection site thrombophlebitis observed in the Phase 1 MAD clinical trial and concern for potential worsening of injection site thrombophlebitis at higher doses with multiple administration, the initial results from animal studies with DT-216P2 using a novel and proprietary excipient, instead of advancing the prior DT-216 product candidate with the current formulation through to Phase 2 in the second half of 2023 as originally planned, we decided to pursue development of DT-216P2 that we believe may better support the future clinical development and regulatory pathway for the drug substance DT-216. We withdrew our IND for the prior DT-216 product candidate in October 2023. We have initiated a Phase 1 SAD clinical trial of DT-216P2 in normal healthy volunteers in Australia to evaluate single doses using multiple routes of administration, specifically IV infusion and SC injection and infusion routes. Results from this Phase 1 SAD clinical trial will inform the design of a clinical trial in FA patients, anticipated to begin in mid-2025. We anticipate providing an update in 2026 on the effect of DT-216P2 on endogenous FXN levels following 12 weeks of dosing. However, there can be no assurance that we will be able to successfully develop DT-216P2 with improved injection site tolerability and the absence of other unacceptable side effects on the timeframe we expect, or at all, or that we will be able to achieve our anticipated timeline for resumed Phase 1 clinical development and data.

If unacceptable side effects, such as severe injection site reactions associated with 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 comparable foreign regulatory authorities may 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 nonclinical studies or clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data.

From time to time, we may publicly disclose interim, preliminary or topline data from our nonclinical studies or clinical trials, which is based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular 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 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 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 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 an infectious disease on patients;
- changes in local regulations as part of a response to a 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 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 nonclinical 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 an 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. 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, HD, 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.

In February 2023, the FDA approved omaveloxolone, a Nrf2 activator, for the treatment of FA in adults and adolescents aged 16 years and older and omaveloxolone was commercially launched by Reata Pharmaceuticals in June 2023. Reata Pharmaceuticals was acquired by Biogen in September 2023. 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 Astellas Pharma Inc, Capsida Biotherapeutics, Solid Biosciences, 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 (licensed from ActualEyes Inc.), 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) Arrowhead Pharmaceuticals evaluating an RNA interference (RNAi) conjugate, (iii) Arthex Biotech evaluating anti-miRNA oligonucleotides, (iv) Avidity Biosciences evaluating an antibody linked siRNA, (v) Dyne Therapeutics evaluating an antibody linked oligonucleotide, (vi) EditForce evaluating an RNA editing technology, (vii) an AAV-based RNA degrading gene therapy by Enzerna Biosciences, (viii) small molecules interacting with RNA under evaluation by Expansion Therapeutics, (ix) Harmony Biosciences evaluating a histamine 3 receptor for the treatment of excessive daytime sleepiness in DM1, (x) Juvena Therapeutics evaluating JUV-161, a stem cell-secreted protein, (xi) Modalis Therapeutics evaluating MDL-202, a gene therapy candidate, (xii) PepGen evaluating a peptide conjugated antisense oligonucleotide, (xiii) Transition Bio evaluating condensate therapeutics, and (xiv) Vertex Pharmaceuticals evaluating a peptide conjugated oligonucleotide (licensed from Entrada Therapeutics).

We are aware of a number of companies with active clinical-stage HD programs including (i) Alnylam Pharmaceuticals evaluating an RNAi therapeutic, (ii) Annexon Biosciences evaluating a monoclonal antibody, (iii) AskBio evaluating AAV delivered cholesterol 24-hydroxylase gene, (iv) Hoffmann-La Roche AG evaluating Tominersen, an antisense oligonucleotide, (v) Prilenia Therapeutics evaluating a sigma-1 receptor agonist, (vi) PTC Therapeutics evaluating a splicing modifier, (vii) Skyhawk Therapeutics evaluating a splicing modifier, (viii) uniQure evaluating an AAV delivered miRNA, (ix) Vaccinex evaluating a monoclonal antibody, (x) VICO evaluating an antisense oligonucleotide, and (xi) Wave Life Sciences evaluating an antisense oligonucleotide.

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, Rocket Pharmaceuticals, Sangamo Biosciences and Verve Therapeutics.

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.

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 clinical trials and perform some of our research and nonclinical 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 nonclinical testing or clinical trials ourselves. As a result, we are and expect to remain dependent on third parties to conduct our nonclinical studies, our ongoing clinical trials 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 nonclinical studies and 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 nonclinical 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 nonclinical studies and clinical trials may be deemed unreliable, and the FDA or comparable foreign regulatory authorities may require us to perform additional nonclinical 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. The 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 an 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 nonclinical 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 nonclinical testing, which are required to conduct nonclinical studies. This has led us to experience increased competition for CRO services, including, without limitation, scheduling nonclinical 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 nonclinical 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 nonclinical 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. For example, as previously announced in May 2023, an unanticipated issue related to the vial stopper used by our vendor for manufacturing the prior DT-216 product candidate caused a short delay in product supply for the Phase 1 MAD clinical trial. In addition, we currently have only one supplier for one of the excipient components of DT-216P2. We may not be able to establish additional sources of supply for this excipient component of DT-216P2 or our other product candidates on a timely basis, or at all, or may be unable to do so on acceptable terms.

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 a 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, including for one of the excipient components of DT-216P2, 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.

Certain Chinese biotechnology companies, CROs and contract development and manufacturing organizations may become subject to trade restrictions, sanctions, other regulatory requirements, or proposed legislation by the U.S. government, which could potentially impact services available for our research and development or our ability to secure the materials we need for our product candidates. For example, the House of Representatives of the prior Congress (the 118th Congress) passed the BIOSECURE Act, which proposed prohibiting U.S. government contracts, grants, and loans to entities that use equipment and services from certain named Chinese biotech companies, and authorizes the U.S. government to name additional Chinese biotechnology companies of concern. The BIOSECURE Act did not become law in the 118th Congress. It is unclear whether the current Congress (the 119th Congress) will introduce the BIOSECURE Act or similar legislation in this congressional session and, if so, how the scope, prohibitions, or designated biotechnology companies of concern may differ from the version of the BIOSECURE Act passed by the House in the prior 118th Congress.

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 nonclinical 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 nonclinical 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 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 nonclinical studies 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. For instance, while DT-216 was generally well-tolerated and exhibited the ability to overcome the FXN transcription impairment that causes FA in the Phase 1 SAD clinical trial and the Phase 1 MAD clinical trial, injection site thrombophlebitis was observed in patients at lower dose levels in the Phase 1 MAD clinical trial. Instead of advancing the prior DT-216 product candidate through to Phase 2 in the second half of 2023 as originally planned, due to concern for potential worsening of injection site thrombophlebitis at higher doses with multiple administration, we decided to pursue development of a potentially improved formulation using a novel and proprietary excipient with DT-216P2 which has shown favorable injection site tolerability that we believe may better support the future clinical development and regulatory pathway for the drug substance, DT-216. We withdrew our IND for the prior DT-216 product candidate in October 2023. We have initiated a Phase 1 SAD clinical trial of DT-216P2 in normal healthy volunteers in Australia to evaluate single doses using multiple routes of administration, specifically IV infusion and SC injection and infusion routes. Results from this Phase 1 SAD clinical trial will inform the design of a clinical trial in FA patients, anticipated to begin in mid-2025. We anticipate providing an update in 2026 on the effect of DT-216P2 on endogenous FXN levels following 12 weeks of dosing. However, there can be no assurance that we will be able to successfully develop DT-216P2 with improved injection site tolerability and the absence of other unacceptable side effects on the timeframe we expect, or at all, or that we will be able to achieve our anticipated timeline for resumed Phase 1 clinical development and data.

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 nonclinical 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 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 claim, 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 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, 2024, we had 54 employees. In addition, we also utilize specialized contract research organizations for additional research and development personnel. Together with our employees, our team comprised approximately 122 full-time equivalents as of December 31, 2024. 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 when needed, we may not be able to successfully implement the tasks necessary to further develop and eventually 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. As of December 31, 2024, we had U.S. federal and state net operating loss (“NOL”) carryforwards of \$86.4 million and \$11.1 million, respectively. U.S. federal NOL carryforwards totaling \$0.1 million begin to expire in 2037, unless previously utilized. The U.S. federal and certain state NOL carryforwards of \$86.3 million and \$0.9 million, respectively, generated after 2017, may be carried forward indefinitely but can only be utilized to offset 80% of future taxable income. The remaining state NOL carryforwards totaling \$10.2 million begin to expire in 2037, unless previously utilized. In addition, we have U.S. federal and state research and development (“R&D”) credit carryforwards totaling \$9.0 million and \$3.2 million, respectively. The U.S. federal R&D credit carryforwards will 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 have experienced additional ownership changes since December 31, 2021, and 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 (HITECH), 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 amendments to and executive, judicial and congressional challenges to certain aspects of the Affordable Care Act. For example, on August 16, 2022, the Inflation Reduction Act of 2022 (Inflation Reduction Act) was signed 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 current 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 and the Consolidated Appropriations Act of 2023, will stay in effect through 2032.

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, the Inflation Reduction Act, among other things, (i) directs the Department of Health and Human Services (HHS) to negotiate the price of certain drugs and biologics that have been on the market for at least 7 years covered under Medicare (the Medicare Drug Price Negotiation Program), 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) imposes 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. HHS has and will continue to issue and update guidance as these programs are implemented. These provisions took effect progressively starting in fiscal year 2023. On August 15, 2024, HHS announced the agreed-upon prices of the first 10 drugs that were subject to price negotiations, although the Medicare drug price negotiation program is currently subject to legal challenges. On January 17, 2025, HHS selected 15 additional drugs covered under Part D for price negotiation in 2025. Each year thereafter more Part B and Part D products will become subject to the Medicare Drug Price Negotiation Program. Further, on December 7, 2023, an initiative to control the price of prescription drugs through the use of march-in rights under the Bayh-Dole Act was announced. On December 8, 2023, the National Institute of Standards and Technology published for comment a Draft Interagency Guidance Framework for Considering the Exercise of March-In Rights which for the first time includes the price of a product as one factor an agency can use when deciding to exercise march-in rights. While march-in rights have not previously been exercised, it is uncertain if that will continue under the new framework.

At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control costs of 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 and the third parties with whom we work are subject to stringent and changing U.S. and foreign laws, regulations and rules, contractual obligations, industry standards, policies and other obligations related to data privacy and security. Our, or our third parties’, actual or perceived failure to comply with such obligations could lead to regulatory investigations or actions, litigation (including class claims) and mass arbitration demands, 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, process) 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 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 governments have enacted numerous data privacy and security laws, including federal health information privacy laws, state data breach notification laws, state health information privacy laws and consumer protection laws (e.g., Section 5 of the Federal Trade Commission Act) and other similar laws (e.g., wiretapping laws). In addition, we obtain health information from certain 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 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.

Numerous U.S. states have enacted comprehensive privacy laws that impose certain obligations on covered businesses, including providing specific disclosures in privacy notices and affording residents with certain rights concerning their personal data. As applicable, such rights may include the right to access, correct, or delete certain personal data, and to opt-out of certain data processing activities, such as targeted advertising, profiling, and automated decision-making. The exercise of these rights may impact our business and ability to provide our products and services to the extent we become subject to these laws in the future. Certain states also impose stricter requirements for processing certain personal data, including sensitive information, such as conducting data privacy impact assessments. These state laws allow for statutory fines for noncompliance. For example, the California Consumer Privacy Act of 2018 (CCPA) applies to personal data of consumers, business representatives, employees and other individuals who are California residents, and requires businesses subject to the CCPA to provide specific disclosures in privacy notices and honor requests of such individuals to exercise certain privacy rights. The CCPA provides for fines and allows private litigants affected by certain data breaches to recover significant statutory damages. 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, should we become subject to them in the future.

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) (collectively, 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 GDPR, companies may face temporary or definitive bans on data processing and other corrective actions; fines up to 20 million Euros under the EU GDPR / 17.5 million pounds sterling under the UK GDPR, or 4% of the annual global revenue, whichever is greater in either case; 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. At this time, we do not believe we are subject to the GDPR, but should this change, the 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.

In Canada, the Personal Information Protection and Electronic Documents Act (PIPEDA) and various related provincial laws, as well as Canada's Anti-Spam Legislation (CASL), may apply to our operations as we expand our clinical trials. Australia's Privacy Act may also apply to our operations as we expand our clinical trials.

Certain jurisdictions have enacted laws requiring data to be localized or limiting the transfer of personal data to other countries. In particular, the EEA and the UK have significantly restricted the transfer of personal data to the United States and other countries whose privacy laws it generally believes are inadequate. Other jurisdictions have adopted similarly stringent data localization and cross-border data transfer laws. 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 EEA standard contractual clauses and the EU-U.S. Data Privacy Framework and UK extension thereto (which allows for transfers to relevant organizations based in the United States who self-certify compliance and participate in the Framework), 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.

Our employees and personnel use generative artificial intelligence (AI) technologies to perform certain tasks at work, and the disclosure and use of personal data in generative AI technologies is subject to various privacy laws and other privacy obligations. Governments have passed and are likely to pass additional laws regulating generative AI. Our use of this technology could result in additional compliance costs, regulatory investigations and actions, and consumer lawsuits. If we are unable to use generative AI, it could make our business less efficient and result in competitive disadvantages.

In addition to data privacy and security laws, we are bound by contractual obligations related to data privacy and security, and our efforts to comply with such obligations may not be successful. 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 publish privacy policies and other statements concerning data privacy, and security. Regulators in the United States are increasingly scrutinizing these statements, and if these policies, materials or statements are found to be deficient, lacking in transparency, deceptive, unfair, misleading, 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 (and consumer data privacy expectations) 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 has, in some instances, prompted 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 include, but are not limited to, government enforcement actions (e.g., investigations, fines, penalties, audits, inspections and similar); litigation (including class-related claims) and mass arbitration demands; additional reporting requirements and/or oversight; bans on processing personal data; orders to destroy or not use personal data; and imprisonment of company officials. In particular, plaintiffs have become increasingly more active in bringing privacy-related claims against companies, including class claims and mass arbitration demands. Some of these claims allow for the recovery of statutory damages on a per violation basis, and, if viable, carry the potential for significant statutory damages, depending on the volume of data and the number of violations. Any of these events could have a material adverse effect on our reputation, business, or financial condition, including but not limited to: 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 product candidates; expenditure of time and resources to defend any claim or inquiry; adverse publicity; or revision or restructuring our operations.

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 product candidates and their uses, platform technologies, 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 will 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. Recent reforms and changes at government agencies of the United States and those of non-U.S. jurisdictions could increase the uncertainties and costs surrounding the prosecution or maintenance of our patent applications, and the maintenance, enforcement, or defense of our issued patents. For example, the ability of the USPTO and other applicable patent authorities to properly administer their functions is highly dependent on the levels of funding available to the agency and their ability to retain key personnel and fill key leadership appointments, among various factors. Termination of employees or delays in replacing or hiring for key positions could significantly impact the ability of the USPTO and other applicable patent authorities to fulfill their functions and could greatly impact our ability to timely and adequately prosecute or maintain our patent applications, and our ability to timely and adequately maintain, enforce, or defend our issued patents. 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 pharmaceutical and biological 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 until issuance of the patent. 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 that 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 issued patents 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, beginning June 1, 2023, European applications and patents may be subjected to the jurisdiction of the Unified Patent Court (UPC). Also, European applications will have the option, upon grant of a patent, of becoming a Unitary Patent which will be subject to the jurisdiction of the 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. As a single court system can invalidate a European patent, we, where applicable, may opt out of the UPC and as such, each European patent would need to be challenged in each individual country.

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 included 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 16, 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 this inventor was the first to invent the claimed invention. As a result, a third party that files a patent application in the USPTO on or after March 16, 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 until publication or 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. We cannot predict how decisions by the federal courts, the U.S. Congress or the USPTO may impact the value of our patent rights. For example, the Supreme Court of the United States held in *Amgen v. Sanofi* (2023) that a functionally claimed genus was invalid for failing to comply with the enablement requirement of the Patent Act. In addition, the Federal circuit recently issued a decision, *In re Cellect, LLC* (2023) involving the interaction of patent term adjustment (PTA), terminal disclaimers, and obvious-type double patenting which may affect the patent term of any issued patents that rely on any PTA. 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. In the 2013 case *Assoc. for Molecular Pathology v. Myriad Genetics, Inc.*, for instance, 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. For example, the Inflation Reduction Act (IRA) passed by Congress authorizes the Secretary of the Department of HHS to negotiate prices directly with participating manufacturers for selected medicines covered by Medicare even if these medicines are protected by an existing patent. For small molecule medicines, the process begins seven years after initial approval by the FDA. While we do not believe that the IRA or its effects will impact our ability to obtain patents in the near future, we cannot be certain whether it will affect our patent strategy in the long run.

Obtaining and maintaining patent protection depends on compliance with various procedural, document submission, 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 are 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 infringing;
- 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, copyrights, 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 nonclinical 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 currently or 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 current or future licensors or collaboration partners. If any of our current or 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 current or future licensors and their counsel that took place prior to the date upon which we assumed control over patent prosecution.

We have entered into and may in the future enter into license agreements with others that may 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 current or 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 current or future licensors may rely on third-party consultants or collaborators or on funds from third parties such that our current or future licensors are not the sole and exclusive owners of the patents we in-license. If other third parties have ownership rights to our current or 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 current or 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 current or 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 current or 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. Additionally, generative AI resources that are publicly available also present a risk that a company may inadvertently obtain, incorporate or use a third party's intellectual property.

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. As a result, we may be unable to identify such patents or patent applications despite our best efforts. 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 product 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-examination, 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, or 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, apply prior to expiration of relevant patents or otherwise satisfy applicable requirements. Administrative changes at the USPTO or other applicable patent authorities, such as reduced hiring and/or funding, may result in delays in issuance of a patent or in accrual of PTE, thereby reducing the amount of PTE that could otherwise be received. Administrative changes (e.g., at the FDA or USPTO) may also lead to delays in review and analysis of requests for PTE, which could result in a PTE not being timely granted (e.g., before the expiration of the patent). If we are unable to obtain PTE or other patent term 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 nonclinical 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, we 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 clinical trials with our current and future product candidates or of our competitors;
- adverse results or delays in nonclinical studies or clinical trials;
- 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 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 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 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 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, consultants, or third parties with whom we work, 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 process proprietary, confidential, and sensitive data (including but not limited to intellectual property, proprietary business information, health-related data, and personal data) (collectively, sensitive information).

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. We and our third-party CROs or other contractors or consultants, are

subject to a variety of evolving threats, including but not limited to social engineering attacks (including through deep fakes, which may be increasingly more difficult to identify as fake, and phishing attacks), malicious code (such as viruses and worms), malware (including as a result of advanced persistent threat intrusions), denial-of-service attacks, credential stuffing or harvesting, ransomware attacks, supply-chain attacks, software bugs, server malfunction, software or hardware failures, loss of data or other information technology assets, adware, telecommunications failures, attacks enhanced or facilitated by AI, 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. It may be difficult and/or costly to detect, investigate, mitigate, contain, and remediate a security incident. Our efforts to do so may not be successful. Actions taken by us or the third parties with whom we work to detect, investigate, mitigate, contain, and remediate a security incident could result in outages, data losses, and disruptions of our business.

Remote work has increased risks to our information technology systems and data, as our employees utilize network connections, computers and devices outside our premises or network, including working at home, while in transit and in public locations. Future or past business transactions (such as acquisitions or integrations) could expose us to additional cybersecurity risks and vulnerabilities, as our systems could be negatively affected by vulnerabilities present in acquired or integrated entities' systems and technologies. Furthermore, we may discover security issues that were not found during due diligence of such acquired or integrated entities, and it may be difficult to integrate companies into our information technology environment and security program.

While we have implemented measures designed to protect against security incidents there can be no assurance that these measures will be effective. We take steps designed to detect, mitigate and remediate vulnerabilities in our information systems (such as our hardware and/or software, including that of third parties upon which we rely). We may not, however, be able to detect and remediate all such vulnerabilities, including on a timely basis. Further, we may experience delays in developing and deploying remedial measures and patches designed to address any such identified vulnerabilities. Vulnerabilities could be exploited and result in a security incident.

We 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 sensitive information. We share or receive sensitive information 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. If the third parties with whom we work experience a security incident or other interruption, which has occurred in the past, we could experience adverse consequences. While we may be entitled to damages if the third parties with whom we work fail to satisfy their privacy or security-related obligations to us, any award may be insufficient to cover our damages, or we may be unable to recover such award.

Any of the previously identified or similar threats could cause a security incident or other interruption, and has in the past. For example, we frequently experience minor phishing attempts and may experience more significant phishing attempts in the future. 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 or conduct clinical trials. 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 require us to implement and maintain specific security measures, industry-standard or reasonable security measures to protect our information technology systems and data.

Applicable data privacy and security obligations as well as public company disclosure obligations may require us, or we may choose, to notify relevant stakeholders, including affected individuals, regulators and investors, of certain security incidents or to take other actions, such as providing credit monitoring and identity protection services. Such disclosures and related actions can be costly, and the disclosures or the failure to comply with applicable requirements could lead to adverse impacts. If we (or a third party with whom we work) experience a

security incident or are perceived to have experienced a security incident, which has occurred in the past, 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 impact our ability to conduct clinical trials or bring any approved products to market, and negatively impact our ability to grow and operate our business. Whether a cybersecurity incident is reportable to our investors may not be straightforward, may take considerable time to determine, and may be subject to change as the investigation of the incident progresses, including changes that may significantly alter any initial disclosure that we provide. Moreover, experiencing a material cybersecurity incident and any mandatory disclosures could lead to negative publicity, loss of investor or partner confidence in the effectiveness of our cybersecurity measures, diversion of management's attention, governmental investigations, lawsuits, and the expenditure of significant capital and other resources.

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.

In addition to experiencing a security incident, third parties may gather, collect, or infer sensitive information about us from public sources, data brokers, or other means that reveals competitively sensitive details about our organization and could be used to undermine our competitive advantage or market position. Additionally, our sensitive information could be leaked, disclosed, or revealed as a result of or in connection with our employees', personnel's, or vendors' use of generative AI technologies.

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, nonclinical 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, disruptions in access to bank deposits or lending commitments due to bank failures and uncertainty about economic stability, 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, including the geopolitical tensions between the U.S. and China, the ongoing Russia/Ukraine conflict and the Israel-Hamas war. 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 1C. Cybersecurity.

Risk management and strategy

We have implemented and maintain various information security processes designed to identify, assess and manage material risks from cybersecurity threats to our critical computer networks, third party hosted services, communications systems, hardware and software, and our critical data, including intellectual property and confidential information that is proprietary, strategic or competitive in nature (Information Systems and Data). Our Chief Operating Officer and our General Counsel help identify, assess and manage our material risks from cybersecurity threats. Along with our Chief Operating Officer and our General Counsel, a third-party information technology strategy and risk reduction vendor helps identify and assess risks from cybersecurity threats by monitoring and evaluating our threat environment and our risk profile using various methods including, for example, manual tools, automated tools, subscribing to reports and services that identify cybersecurity threats, analyzing reports of threats and actors, conducting scans of the threat environment, evaluating our and our industry's risk profile, evaluating threats reported to us, internal audits, conducting threat assessments for internal and external threats, conducting vulnerability assessments to identify vulnerabilities, use of external intelligence feeds and coordinating with law enforcement as appropriate about certain threats.

Depending on the environment, we implement and maintain various technical, physical, and organizational measures, processes, standards and policies designed to manage and mitigate material risks from cybersecurity threats to our Information Systems and Data, including, for example: incident detection and response procedures; an incident response policy; a vulnerability management policy; conducting risk assessments; encrypting certain of our data; maintaining network security controls; segmenting certain of our data; maintaining access and physical security controls; asset management, tracking, and disposal protocols; systems monitoring; vendor risk management processes; employee training; maintaining cybersecurity insurance; and retaining a third party information technology strategy and risk reduction vendor.

Our assessment and management of material risks from cybersecurity threats are integrated into our overall risk management processes. For example, cybersecurity risk is addressed as a component of our enterprise risk management program; our Chief Operating Officer and General Counsel work with management to prioritize our risk management processes and mitigate cybersecurity threats that are expected to be more likely to lead to a material impact to our business; our Chief Operating Officer and General Counsel evaluate material risks from cybersecurity threats against our overall business objectives and our Chief Operating Officer reports to the audit committee of the board of directors, which evaluates our overall enterprise risk.

We use third-party service providers to assist us from time to time to identify, assess, and manage material risks from cybersecurity threats, including for example, professional services firms (including outside legal counsel), threat intelligence service providers, cybersecurity consultants, cybersecurity software providers, managed cybersecurity service providers, and dark web monitoring services.

We use third-party service providers to perform a variety of functions throughout our business, such as application providers, hosting services, contract research organizations and contract manufacturing organizations. We have vendor management processes to identify and oversee cybersecurity risks associated with the use of our providers. Depending on the nature of the services provided, the sensitivity of the Information Systems and Data at issue, and the identity of the provider, these processes may include a risk assessment of the vendor, security

questionnaire, security assessments, security assessment calls with the vendor's security personnel and imposition of contractual obligations on the vendor.

For a description of the risks from cybersecurity threats that may materially affect us and how they may do so, see our risk factors under Part I. Item 1A. Risk Factors in this Annual Report on Form 10-K, including "Our information technology systems or sensitive data, or those of our third-party CROs or other contractors or consultants, or third parties with whom we work, 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."

Governance

Our board of directors addresses our cybersecurity risk management as part of its general oversight function. The board of directors' audit committee is responsible for overseeing our cybersecurity risk management processes.

Our cybersecurity risk assessment and management processes are implemented and maintained by certain of our management, including our Chief Operating Officer and our General Counsel. Our Chief Operating Officer has been responsible for the oversight of our cybersecurity since he joined our company in May 2019. He has a B.A. in Computer Science. Our General Counsel has oversight of our legal department, has prior experience serving as inside and outside corporate counsel to technology and cybersecurity companies and a highly regulated cancer diagnostics company.

Our cybersecurity incident response and vulnerability management processes are designed to escalate certain cybersecurity incidents to members of management depending on the circumstances, including our Chief Operating Officer and our General Counsel. Our Chief Operating Officer and our General Counsel will work with our incident response team to help us mitigate and remediate cybersecurity incidents of which they are notified. In addition, our incident response processes include reporting to the audit committee of the board of directors for certain cybersecurity incidents.

The audit committee receives periodic reports from our Chief Operating Officer concerning our significant cybersecurity threats and risk and the processes we have implemented to address them. The audit committee also receives and has access to various reports, summaries or presentations related to cybersecurity threats, risk and mitigation.

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 is listed on the Nasdaq Global Select Market under the symbol "DSGN".

Holders of Common Stock

As of March 6, 2025, there were 56,762,678 shares of common stock issued and held by approximately 11 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.

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, 2024, we had used approximately \$102.5 million of the net proceeds received from our initial public offering to support our operations.

Pending their use, the remaining 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.

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's disease (HD), the nucleotide repeat expansions result in the generation of toxic gene products, often associated with pathological nuclear foci and broad splicing disruptions or the expression of mutant proteins that form toxic aggregates. 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 (NHPs), 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[®] small molecule, DT-216, formulated as the prior DT-216 product candidate, was cleared by the U.S. Food and Drug Administration (FDA) to commence Phase 1 clinical trials. In December 2022, we reported positive initial data from the Phase 1 single-ascending dose (SAD) clinical trial and in August 2023, we reported data from the Phase 1 multiple-ascending dose (MAD) clinical trial of the prior DT-216 product candidate. Both studies showed that DT-216 was generally well-tolerated and exhibited the ability to overcome the FXN transcription impairment that causes FA. Data from the Phase 1 MAD clinical trial suggests more sustained exposure is likely needed to achieve a more durable increase in FXN expression, and we observed five cases of injection site thrombophlebitis in the Phase 1 MAD clinical trial. We then shifted focus to developing DT-216 with a potentially improved formulation to enable higher exposure and chronic administration for treatment of FA. These efforts resulted in a new product candidate, DT-216P2, which uses the same drug substance, DT-216. In nonclinical studies, we observed higher and more sustained DT-216 plasma levels after administration of DT-216P2 than was seen in studies with the prior DT-216 product candidate. Additionally, we observed favorable injection site tolerability following multiple intravenous (IV) administrations of DT-216P2. We have initiated a Phase 1 SAD clinical trial of DT-216P2 in normal healthy volunteers in Australia to evaluate single doses using multiple routes of administration, specifically IV infusion and subcutaneous (SC) injection and infusion routes. Results from this Phase 1 SAD clinical trial will inform the design of a clinical trial in FA patients, anticipated to begin in mid-2025. We anticipate providing an update in 2026 on the effect of DT-216P2 on endogenous FXN levels following 12 weeks of dosing.

In December 2022, we nominated our second GeneTAC[®] small molecule, 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. We have completed dosing in a Phase 1 clinical trial in normal healthy volunteers to evaluate the safety of DT-168 and plan to provide results in the first half of 2025. In addition, DT-168 has been evaluated in chronic toxicity studies of up to nine months in duration. We are currently conducting an observational study in FECD to confirm disease characteristics and evaluate deterioration in the context of running a trial and to identify characteristics of FECD patients at risk of more rapid disease progression. We have achieved our enrollment goal for the observational study by recruiting and completing baseline assessments on approximately 250 FECD patients. Based on the baseline characteristics data, we have chosen approximately 100 patients for future follow-up visits. This will inform our clinical development efforts and we believe it could potentially increase the probability of DT-168 programmatic success.

Our third program based on the GeneTAC[®] platform is focused on DM1. 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 in DM1 patients. We plan to continue evaluating the properties of our DM1 GeneTAC[®] molecules in preclinical studies in order to nominate a development candidate in 2025.

Our fourth program based on the GeneTAC[®] platform is focused on HD. We are currently conducting preclinical studies on promising HD GeneTAC[®] candidate molecules. We have observed reduced mutant huntingtin (mtHTT) mRNA and protein and preservation of wild type huntingtin (wtHTT) in HD patient cells after treatment with our HD GeneTAC[®] candidate molecules. In *in vivo* studies in zQ175DN mice, an animal model of HD, we observed a reduction of over 50% in mtHTT mRNA and protein in the brain striatum after eight weeks of systemic administration of our HD GeneTAC[®] candidate molecules. In the same study, wtHTT mRNA and protein levels were shown to be preserved after treatment with our HD GeneTAC[®] candidate molecules. We plan to continue to evaluate these HD candidate molecules in nonclinical studies. The final development candidate will be based on the molecules that perform favorably in relevant studies.

We have continued to make significant progress in advancing our GeneTAC[®] portfolio in preclinical studies to address other 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.

To date, we have incurred net losses and negative cash flows from operations since our inception and as of December 31, 2024, had an accumulated deficit of \$227.2 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 nonclinical 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 nonclinical 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, 2024, was \$245.5 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, nonclinical development and manufacturing of our product candidates and our discovery efforts. Research and development expenses are recognized as incurred.

Direct costs include:

- external research and development expenses incurred under agreements with contract research organizations, consultants and other vendors that conduct our clinical, nonclinical and discovery activities;
- expenses related to manufacturing our product candidates for clinical and nonclinical 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 rent, 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, nonclinical 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 increase for the foreseeable future as we continue the development of our FA, FECD, DM1 and HD programs and our other discovery programs, in particular as we advance our product candidates into and through clinical development. As of the date of this Annual Report on Form 10-K, we cannot reasonably determine with certainty the timing of initiation of future clinical trials, or the duration or completion costs of our current or future nonclinical studies and clinical programs, for our product candidates due to the inherently unpredictable nature of nonclinical and clinical development. Nonclinical 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 nonclinical 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, nonclinical and clinical 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 scope and costs of designing and implementing drug product improvements (including alternate formulations) and manufacturing our product candidates;
- 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 nonclinical 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, 2024 and 2023

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

	Year Ended December 31,		
	2024	2023	Change
Operating expenses:			
Research and development	\$ 44,350	\$ 57,063	\$ (12,713)
General and administrative	18,033	21,127	(3,094)
Total operating expenses	\$ 62,383	\$ 78,190	\$ (15,807)

Research and Development Expenses. The decrease in direct research and development expenses in 2024 compared to 2023 was primarily due to completion of clinical activities for our FA program in 2023. Expenses associated with our early-stage programs, that are not allocated on a program-by-program basis, decreased due to the breakout of the FECD program, which moved into clinical development. The decrease in indirect research and development expenses compared to 2023 was primarily due to lower headcount, resulting in a \$1.7 million decrease in personnel-related costs inclusive of stock-based compensation, a \$1.2 million decrease in laboratory and related supplies, a \$2.2 million decrease in indirect research that benefits multiple early-stage programs and a \$0.2 million decrease in other expenses.

The following table summarizes our research and development expenses by direct and indirect costs for the year ended December 31, 2024 and 2023 (in thousands):

	Year Ended December 31,		
	2024	2023	Change
FA	\$ 8,559	\$ 16,159	\$ (7,600)
FECD	5,271	—	5,271
Other direct	10,849	15,889	(5,040)
Indirect	19,671	25,015	(5,344)
Total research and development expense	\$ 44,350	\$ 57,063	\$ (12,713)

General and Administrative Expenses. The decrease in general and administrative expenses in 2024 compared to 2023 was primarily due to lower headcount, resulting in a \$2.3 million decrease in personnel-related costs inclusive of stock-based compensation, a \$0.6 million decrease in professional services and a \$0.2 million decrease in other expenses.

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. As of December 31, 2024, we had \$245.5 million of combined cash and cash equivalents and investment securities, a decrease of \$36.3 million from the \$281.8 million of cash and cash equivalents and investment securities at December 31, 2023. The following table summarizes our cash flow activities (in thousands):

	Year Ended December 31,	
	2024	2023
Net cash (used in) provided by:		
Operating activities	\$ (43,105)	\$ (58,560)
Investing activities	43,955	52,536
Financing activities	513	724
Net increase (decrease) in cash and cash equivalents	\$ 1,363	\$ (5,300)

Operating Activities. The decrease in our net cash used in operating activities was primarily due to the \$17.3 million decrease in net loss, partially offset by an increase in net working capital for the year ended December 31, 2024 compared to the same period of the prior year. The lower net loss incurred during the 2024 period was primarily due to decreased expenses related to our FA program and lower personnel-related costs.

Investing Activities. The decrease in net cash provided by investing activities was primarily due to a net decrease in cash provided from the maturities and purchases of our investment securities during the year ended December 31, 2024 compared to the year ended December 31, 2023. We have classified our investment securities as available-for-sale and all investments are made in accordance with our investment policy.

Financing Activities. Net cash provided by financing activities for each of the years ended December 31, 2024 and 2023 was comprised of proceeds received from the issuance of common stock through our employee stock purchase plan and from employee stock option exercises.

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. As of December 31, 2024, the Company has not sold any shares of its common stock under the ATM Program.

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, nonclinical 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 designing and implementing drug product improvements (including alternate formulations) and 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, European Medicines Agency (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 our current and 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 additional laboratory space; 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 (such as the geopolitical tensions between the U.S. and China, the ongoing Russia/Ukraine conflict and the Israel-Hamas war), inflation, tariffs, bank failures, global supply chain and labor shortage challenges, and the effects of a 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 \$100,000 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. The Company will recognize these milestone payments and royalties when paid or payable. There were no additional payments or royalties recorded through December 31, 2024.

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 each of the years ended December 31, 2024 and 2023.

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.

In May 2024, we entered into a license agreement pursuant to which we received exclusive, worldwide, royalty-bearing, sublicensable rights to certain patents and technology to be used in the development and commercialization of certain products. We paid \$0.2 million in license fees during the year ended December 31, 2024, which was expensed to research and development as there is no alternative future use for the license.

We may be obligated to make aggregate regulatory milestone payments of up to \$0.8 million for each product incorporating licensed patent rights and pay a royalty on worldwide net sales on a product-by-product basis. The Company will recognize these milestone payments and royalties when paid or payable. There were no additional payments or royalties recorded through December 31, 2024.

We may terminate the license agreement with 60 days' written notice and each party may terminate the license agreement upon 30 days' written notice for certain breaches of the agreement that remain uncured following 60 days' notice to the other party of such breach. Unless terminated earlier by the parties, the term of the license agreement will continue until the last valid patent claim expires.

Additionally, we enter into agreements in the normal course of business with third-party vendors for nonclinical 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 nonclinical 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 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 Part II, Item 8, “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.

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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, 2024 and 2023, the related statements of operations, comprehensive loss, stockholders' equity and cash flows for each of the two years in the period ended December 31, 2024, 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, 2024 and 2023, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2024, 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 10, 2025

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

	December 31, 2024	December 31, 2023
Assets		
Current assets:		
Cash and cash equivalents	\$ 22,563	\$ 21,200
Investment securities	222,914	260,598
Prepaid expenses and other current assets	2,563	2,786
Total current assets	248,040	284,584
Property and equipment, net	1,410	1,691
Right-of-use asset, related party	2,216	2,938
Other assets	427	430
Total assets	<u>\$ 252,093</u>	<u>\$ 289,643</u>
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	\$ 2,186	\$ 1,940
Accrued expenses and other current liabilities (including related party amounts of \$800 and \$716, respectively)	6,276	7,682
Total current liabilities	8,462	9,622
Operating lease liability, net, related party	1,534	2,334
Total liabilities	9,996	11,956
Commitments and contingencies (See Note 11)		
Stockholders' equity:		
Common stock: \$0.0001 par value; 200,000,000 shares authorized, 56,754,341 and 56,473,598 shares issued and outstanding at December 31, 2024 and 2023, respectively	6	6
Additional paid-in capital	468,830	455,245
Accumulated deficit	(227,214)	(177,626)
Accumulated other comprehensive income	475	62
Total stockholders' equity	242,097	277,687
Total liabilities and stockholders' equity	<u>\$ 252,093</u>	<u>\$ 289,643</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)

	Year Ended December 31,	
	2024	2023
Operating expenses:		
Research and development (including related party amounts of \$891 and \$991, respectively)	\$ 44,350	\$ 57,063
General and administrative (including related party amounts of \$537 and \$538, respectively)	18,033	21,127
Total operating expenses	62,383	78,190
Loss from operations	(62,383)	(78,190)
Interest income	12,795	11,328
Net loss	\$ (49,588)	\$ (66,862)
Net loss per share, basic and diluted	\$ (0.88)	\$ (1.19)
Weighted-average shares of common stock outstanding, basic and diluted	56,587,142	55,984,670

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,	
	2024	2023
Net loss	\$ (49,588)	\$ (66,862)
Other comprehensive loss:		
Unrealized gain on available-for-sale securities	413	3,418
Comprehensive loss	\$ (49,175)	\$ (63,444)

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

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

	Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive (Loss) Income	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount				
Balance at December 31, 2022	55,895,596	\$ 6	\$ 441,424	\$ (3,356)	\$ (110,764)	\$ 327,310
Exercises of stock options and vesting of restricted stock	492,116	—	428	—	—	428
Issuance of common stock under employee stock purchase plan	85,886	—	305	—	—	305
Stock-based compensation	—	—	13,088	—	—	13,088
Unrealized gain on investments	—	—	—	3,418	—	3,418
Net loss	—	—	—	—	(66,862)	(66,862)
Balance at December 31, 2023	56,473,598	\$ 6	\$ 455,245	\$ 62	\$ (177,626)	\$ 277,687
Exercises of stock options	37,133	—	36	—	—	36
Issuance of common stock under employee stock purchase plan	243,610	—	477	—	—	477
Stock-based compensation	—	—	13,072	—	—	13,072
Unrealized gain on investments	—	—	—	413	—	413
Net loss	—	—	—	—	(49,588)	(49,588)
Balance at December 31, 2024	56,754,341	\$ 6	\$ 468,830	\$ 475	\$ (227,214)	\$ 242,097

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

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

	Year Ended December 31,	
	2024	2023
Cash flows from operating activities		
Net loss	\$ (49,588)	\$ (66,862)
Reconciliation of net loss to net cash used in operating activities:		
Depreciation	596	537
Stock-based compensation	13,072	13,088
Amortization of premiums on investment securities, net	(6,198)	(6,084)
Non-cash lease expense	6	33
Change in operating assets and liabilities:		
Prepaid expense and other assets	226	1,974
Accounts payable and other liabilities	(1,219)	(1,246)
Net cash used in operating activities	(43,105)	(58,560)
Cash flows from investing activities		
Purchases of investment securities	(230,175)	(224,703)
Proceeds from maturities of investment securities	274,470	277,495
Purchases of property and equipment	(340)	(256)
Net cash provided by investing activities	43,955	52,536
Cash flows from financing activities		
Proceeds from the exercise of stock options	36	419
Issuance of common stock through employee stock purchase plan	477	305
Net cash provided by financing activities	513	724
Net decrease in cash and cash equivalents	1,363	(5,300)
Cash and cash equivalents at beginning of period	21,200	26,500
Cash and cash equivalents at end of period	\$ 22,563	\$ 21,200
Supplemental disclosures		
Purchases of property and equipment included in accrued expenses	\$ —	\$ 25

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 GeneTAC[®] programs to address other diseases.

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 \$227.2 million as of December 31, 2024. The Company had cash, cash equivalents and investment securities of \$245.5 million as of December 31, 2024, 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, 2024 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 (“CODM”) in making decisions regarding resource allocation and assessing performance. The Company operates in one operating and reportable segment, Design Therapeutics, Inc., which is focused on utilizing the Company’s proprietary GeneTAC[®] platform to design and develop therapeutic candidates for inherited diseases driven by nucleotide repeat expansion.

The Company’s CODM is its Chief Executive Officer. The CODM manages the Company’s operations as one segment for the purposes of assessing performance and making operating decisions. The Company’s management of segment profit or loss and assets are evaluated at the consolidated level, and it manages its research activities on a consolidated basis.

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 years 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, 2024 and 2023.

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 accounts for lease and non-lease components as a single lease component. 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.

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.

Recent Accounting Pronouncements

In November 2023, the Financial Accounting Standards Board (“FASB”) issued ASU 2023-07, Accounting Standards Codification (“ASC”) Topic 280, *Segment Reporting: Improvements to Reportable Segment Disclosures*, which expands annual and interim disclosure requirements for reportable segments, primarily through enhanced disclosures about significant segment expenses. The ASU also requires public entities with a single reportable segment to provide all segment disclosures under ASC 280, including the new disclosures under the ASU. Annual disclosures are required for fiscal years beginning after December 15, 2023 and for interim disclosures within fiscal years beginning after December 15, 2024. Retrospective application is required. The Company adopted the standard for the year ended December 31, 2024. The impact of the adoption of the amendments in this update was not material to the Company’s financial position and results of operations, as the requirements impact only segment reporting disclosures in the Company’s notes to financial statements.

In December 2023, the FASB issued ASU 2023-09, ASC Topic 740, *Income Taxes: Improvements to Income Tax Disclosures*, which requires disaggregated information about a reporting entity’s effective tax rate reconciliation as well as information on income taxes paid. ASU 2023-09 is effective for fiscal years beginning after December 15, 2024, with early adoption permitted. The Company is currently evaluating ASU 2023-09 and does not expect it to have a material effect on its financial statement disclosures.

In November 2024, the FASB issued Accounting Standard Update (“ASU”) 2024-03, *Income Statement - Reporting Comprehensive Income - Expense Disaggregation Disclosures (Subtopic 220-40): Disaggregation of Income Statement Expenses*, which is intended to enhance transparency into the nature and function of expenses. The amendments require that on an annual and interim basis, entities disclose disaggregated operating expense information about specific expense categories. The amendments are effective for fiscal years beginning after December 15, 2026, and for interim periods within fiscal years beginning after December 15, 2027. Early adoption is permitted and the amendments may be applied either prospectively or retrospectively. The Company is currently evaluating the impact that the updated standard will have on its financial statement disclosures.

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 method. Dilutive common stock equivalents are comprised of stock options outstanding under the Company’s equity incentive plans 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:

	December 31, 2024	December 31, 2023
Stock options	10,328,177	8,561,753
Employee stock purchase plan	70,492	19,907
Total	10,398,669	8,581,660

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, 2024 and 2023 (in thousands):

	Fair Value Measurement at End of Period Using:			
		Quoted Prices In Active Markets For Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Total				
As of December 31, 2024:				
Assets:				
Money market funds ⁽¹⁾	\$ 20,800	\$ 20,800	\$ —	\$ —
Certificates of deposit	2,898	2,898	—	—
U.S. Treasury securities	197,528	197,528	—	—
U.S. Government agency securities	22,488	—	22,488	—
Total	<u>\$ 243,714</u>	<u>\$ 221,226</u>	<u>\$ 22,488</u>	<u>\$ —</u>
As of December 31, 2023:				
Assets:				
Money market funds ⁽¹⁾	\$ 19,619	\$ 19,619	\$ —	\$ —
Certificates of deposit	14,336	14,336	—	—
U.S. Treasury securities	221,304	221,304	—	—
U.S. Government agency securities	24,958	—	24,958	—
Total	<u>\$ 280,217</u>	<u>\$ 255,259</u>	<u>\$ 24,958</u>	<u>\$ —</u>

⁽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. The Company obtains the fair value of its available-for-sale debt securities from a professional pricing service. Level II securities are valued using quoted market prices for similar instruments, non-binding market prices that are corroborated by observable market data and include our investments in marketable debt instruments of government sponsored enterprises.

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. The Company's investment securities consisted of the following at December 31, 2024 and 2023 (in thousands):

As of December 31, 2024						
	Maturity	Amortized Cost	Unrealized Gains	Unrealized Losses	Allowance for Credit Losses	Estimated Fair Market Value
Certificates of deposits	Within 1 year	\$ 2,884	\$ 14	\$ —	\$ —	\$ 2,898
U.S. Treasury securities	Within 1 year	172,178	391	—	—	172,569
U.S. Government agency securities	Within 1 year	7,500	—	(7)	—	7,493
U.S. Treasury securities	Greater than 1 year	24,878	83	(2)	—	24,959
U.S. Government agency securities	Greater than 1 year	14,999	1	(5)	—	14,995
Total		<u>\$ 222,439</u>	<u>\$ 489</u>	<u>\$ (14)</u>	<u>\$ —</u>	<u>\$ 222,914</u>

As of December 31, 2023						
	Maturity	Amortized Cost	Unrealized Gains	Unrealized Losses	Allowance for Credit Losses	Estimated Fair Market Value
Certificates of deposits	Within 1 year	\$ 10,488	\$ 2	\$ (23)	\$ —	\$ 10,467
U.S. Treasury securities	Within 1 year	162,746	70	(349)	—	162,467
U.S. Government agency securities	Within 1 year	12,499	—	(29)	—	12,470
Certificates of deposits	1 year to 2 years	3,862	12	(5)	—	3,869
U.S. Treasury securities	1 year to 2 years	58,441	412	(16)	—	58,837
U.S. Government agency securities	1 year to 2 years	12,500	2	(14)	—	12,488
Total		<u>\$ 260,536</u>	<u>\$ 498</u>	<u>\$ (436)</u>	<u>\$ —</u>	<u>\$ 260,598</u>

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.

There were 12 and 71 securities in an unrealized loss position at December 31, 2024 and 2023, respectively. The Company determined that unrealized losses on its available-for-sale investment securities were primarily attributable to changes in interest rates. Each security remained at a high credit quality rating. Further, there had

been no adverse conditions noted for any of the issuers and the Company does not intend to sell any of the securities prior to maturity. As such, an allowance for credit losses has not been recognized as of December 31, 2024 or 2023.

The following tables present available-for-sale investments that were in an unrealized loss position as of December 31, 2024 and 2023, aggregated by security type and length of time in a continuous unrealized loss position (in thousands):

	As of December 31, 2024					
	Less than 12 Months		12 Months or Greater		Total	
	Estimated Fair Market Value	Unrealized Losses	Estimated Fair Market Value	Unrealized Losses	Estimated Fair Market Value	Unrealized Losses
Certificates of deposits	\$ —	\$ —	\$ 490	\$ —	\$ 490	\$ —
U.S. Treasury securities	7,514	(2)	—	—	7,514	(2)
U.S. Government agency securities	19,987	(12)	—	—	19,987	(12)
Total	<u>\$ 27,501</u>	<u>\$ (14)</u>	<u>\$ 490</u>	<u>\$ —</u>	<u>\$ 27,991</u>	<u>\$ (14)</u>

	As of December 31, 2023					
	Less than 12 Months		12 Months or Greater		Total	
	Estimated Fair Market Value	Unrealized Losses	Estimated Fair Market Value	Unrealized Losses	Estimated Fair Market Value	Unrealized Losses
Certificates of deposits	\$ 8,514	\$ (14)	\$ 1,456	\$ (14)	\$ 9,970	\$ (28)
U.S. Treasury securities	44,346	(102)	51,979	(263)	96,325	(365)
U.S. Government agency securities	12,484	(16)	7,473	(27)	19,957	(43)
Total	<u>\$ 65,344</u>	<u>\$ (132)</u>	<u>\$ 60,908</u>	<u>\$ (304)</u>	<u>\$ 126,252</u>	<u>\$ (436)</u>

As of December 31, 2024, the Company held 12 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 “Prepaid expenses and other current assets” on the Company’s balance sheets, was \$1.3 million and \$1.4 million at December 31, 2024 and 2023, respectively.

6. Balance Sheet Details

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

	December 31, 2024	December 31, 2023
Prepaid expenses	\$ 1,300	\$ 1,354
Interest receivable	1,263	1,432
Total	<u>\$ 2,563</u>	<u>\$ 2,786</u>

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

	December 31, 2024	December 31, 2023
Laboratory equipment	\$ 2,291	\$ 1,976
Computer equipment and software	102	102
Furniture and fixtures	521	521
Leasehold improvements	151	151
	<u>3,065</u>	<u>2,750</u>
Less accumulated depreciation	<u>(1,655)</u>	<u>(1,059)</u>
Total	<u>\$ 1,410</u>	<u>\$ 1,691</u>

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

	December 31, 2024	December 31, 2023
Accrued personnel costs	\$ 3,576	\$ 4,034
Accrued research and development costs	1,220	2,350
Current portion of operating lease liability, related party	800	716
Accrued other	680	582
Total	<u>\$ 6,276</u>	<u>\$ 7,682</u>

7. Leases

In February 2021, the Company entered into a lease agreement with Crossing Holdings, LLC to rent office space (the “Lease”). Dr. Pratik Shah and entities that he controls are the sole members 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 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, 2024, the weighed-average remaining lease term for the Company's leases was 2.7 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, 2024 are as follows (in thousands):

2025	\$ 945
2026	973
2027	663
Total future minimum lease payments	2,581
Less: Present value adjustment	(247)
Operating lease liabilities, related party	<u>\$ 2,334</u>

Rent expense was \$0.9 million for each of the years ended December 31, 2024 and 2023.

8. Stockholders’ Deficit

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, 2024, the Company has not sold any shares of its common stock under the ATM Program.

9. Stock-Based Compensation

Equity Incentive Award Plans

In March 2021, the Company adopted the 2021 Plan. 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, 2024, the Company had 6,122,854 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 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, 2025, the number of shares available for future issuance was increased by 2,837,717 shares so that the total available for future issuance as of January 1, 2025 was 8,960,571 shares.

In August 2023, the Company granted two stock options, each to purchase up to 525,000 shares of the Company's common stock, which contain both time-based and performance-based conditions. The options have a weighted average grant date fair value of \$1.64 per share. Stock-based compensation expense for awards with performance conditions is recognized straight-line over the expected performance period when the achievement of such performance conditions is determined to be probable. The Company assessed the probability of achieving the performance-based conditions and recorded approximately \$0.2 million and \$0.1 million in general and administrative stock-based compensation expense during the years ended December 31, 2024 and 2023, respectively.

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, 2023	8,561,753	\$ 8.67	8.46	\$ 1,115,560
Granted	2,818,450	\$ 2.81		
Exercised	(37,133)	\$ 0.95		
Canceled/Expired	(1,014,893)	\$ 10.13		
Outstanding at December 31, 2024	10,328,177	\$ 6.96	7.86	\$ 19,649,110
Vested and expected to vest at December 31, 2024	9,678,177	\$ 7.26	7.80	\$ 17,254,360
Exercisable at December 31, 2024	4,332,597	\$ 9.76	6.88	\$ 4,958,068

The weighted-average grant date fair value per share of options granted was \$2.11 and \$3.45 for the years ended December 31, 2024 and 2023, respectively. The aggregate intrinsic value of options exercised was \$0.1 million and \$0.7 million for the years ended December 31, 2024 and 2023, respectively, and the cash received from options exercised was \$36,000 and \$0.4 million for the years ended December 31, 2024 and 2023, respectively.

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,	
	2024	2023
Expected term (years)	6.11	6.10
Expected volatility	87.0%	70.0%
Risk-free interest rate	3.93%	3.87%
Expected dividend yield	0.0%	0.0%

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

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 adopted the ESPP. 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.

As of December 31, 2024, the Company had issued 376,386 shares of the Company's common stock under the ESPP and had 1,904,599 shares available for future issuance. 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 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, 2025, the number of shares available for issuance was increased by 567,543 shares so that the total available for future issuance as of January 1, 2025 was 2,472,142 shares.

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, 2024, were as follows:

	Year Ended December 31,	
	2024	2023
Expected term (years)	1.39	1.51
Expected volatility	88.9%	85.4%
Risk-free interest rate	4.82%	4.44%
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,	
	2024	2023
Research and development	\$ 6,575	\$ 6,152
General and administrative	6,497	6,936
Total	<u>\$ 13,072</u>	<u>\$ 13,088</u>

As of December 31, 2024, unrecognized compensation expense related to unvested stock option awards was \$17.1 million, which is expected to be recognized in expense over a weighted-average period of 1.3 years. As of December 31, 2024, unrecognized compensation expense related to ESPP rights was \$0.5 million, which is expected to be recognized over a remaining period of 1.9 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, 2024 or 2023, and has not recognized interest or penalties in its statements of operations and comprehensive loss for the years ended December 31, 2024 and 2023, respectively. Further, the Company is not currently under examination by any federal, state or local tax authority.

At December 31, 2024, the Company had federal and state net operating loss ("NOL") carryforwards of \$86.4 million and \$11.1 million, respectively. Federal NOL carryforwards totaling \$0.1 million begin to expire in 2037, unless previously utilized. The federal and certain state NOL carryforwards of \$86.3 million and \$0.9 million, respectively, generated after 2017, may be carried forward indefinitely but can only be utilized to offset 80% of future taxable income. The remaining 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 \$9.0 million and \$3.2 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, 2021 would expire solely as a result of annual limitations on the utilization of those attributes. If ownership changes occurred after December 31, 2021 or 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, 2024 and 2023 were as follows (in thousands):

	December 31, 2024	December 31, 2023
Deferred tax assets:		
Net operating losses	\$ 18,885	\$ 15,074
Capitalized research costs	20,545	16,635
Research and development credits	9,352	6,996
Lease liability	492	641
Stock-based compensation	3,908	3,255
Other	797	810
Total gross deferred tax assets	53,979	43,411
Valuation allowance	(53,143)	(42,436)
Total deferred tax assets	836	975
Deferred tax liabilities:		
Right of use asset	(467)	(618)
Other	(369)	(357)
Total deferred tax liabilities	(836)	(975)
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, 2024	December 31, 2023
Expected tax benefit at federal statutory rate	\$ (10,413)	\$ (14,042)
State income taxes, net of federal benefit	(34)	(37)
Research and development credits	(2,354)	(3,722)
Stock-based compensation	1,310	906
162(m) officer's compensation	799	383
Other	(102)	132
Change in valuation allowance	10,794	16,380
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, 2024	December 31, 2023
Balance at beginning of period	\$ 1,799	\$ 929
Increase (decrease) related to prior year tax positions	(3)	87
Increase to current year tax positions	493	783
Decreases due to settlements	—	—
Expiration of the statute of limitations for the assessment of taxes	—	—
Balance at end of period	<u>\$ 2,289</u>	<u>\$ 1,799</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, 2024 or December 31, 2023.

12. License Agreements

In May 2024, the Company entered into a license agreement pursuant to which it received exclusive, worldwide, royalty-bearing, sublicensable rights to certain patents and technology to be used in the development and commercialization of certain products. The Company paid \$0.2 million in license fees during the year ended December 31, 2024, which was expensed to research and development as there is no alternative future use for the license.

The Company may be obligated to make aggregate regulatory milestone payments of up to \$0.8 million for each product incorporating licensed patent rights and pay a royalty on worldwide net sales on a product-by-product basis. The Company will recognize these milestone payments and royalties when paid or payable. There were no additional payments or royalties recorded through December 31, 2024.

The Company may terminate the license agreement with 60 days' written notice and each party may terminate the license agreement upon 30 days' written notice for certain breaches of the agreement that remain uncured following 60 days' notice to the other party of such breach. Unless terminated earlier by the parties, the term of the license agreement will continue until the last valid patent claim expires.

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.

In 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 will recognize these milestone payments and royalties when paid or payable. There were no additional payments or royalties recorded through December 31, 2024.

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 immaterial for the years ended December 31, 2024 and 2023.

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. Dr. Pratik Shah and entities that he controls are the sole members of Crossing Holdings, LLC.

Rent, and related operating expenses recognized by the Company under the Lease and Lease Amendment during the periods presented were as follows (in thousands):

	Year Ended December 31,	
	2024	2023
Research and development	\$ 848	\$ 845
General and administrative	297	298
Total expenses	<u>\$ 1,145</u>	<u>\$ 1,143</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 Chief Executive Officer and Chairperson 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,	
	2024	2023
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., a co-founder, to provide consulting services and advise on certain research and development activities (the “Research Consulting Agreement”). Pursuant to the Research Consulting Agreement, as amended, Dr. Ansari performed these services for a monthly fee of \$15,000. In November 2023, the Company further amended the Research Consulting Agreement, discontinued the monthly fee effective October 1, 2023 and granted Dr. Ansari an option to purchase 100,000 shares of the Company's common stock. The option has a grant date fair value of \$1.72 per share and is being expensed to research and development over a four-year vesting period. The Company recorded approximately \$43,000 and \$11,000 in related stock-based compensation expense during the years ended December 31, 2024 and 2023, respectively.

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

	Year Ended December 31,	
	2024	2023
Research and development	\$ 43	\$ 146
Total expenses	<u>\$ 43</u>	<u>\$ 146</u>

14. Segment Information

The Company manages the business activities at the consolidated level and operates in one operating and reportable segment.

The Company's CODM is its chief executive officer. The CODM primarily utilizes long-range financial projections and cash runway in order to allocate resources and to assess performance. As of December 31, 2024, the Company has no revenue and all the Company's long-lived assets were located within the United States.

	Twelve months ended December 31,	
	2024	2023
Interest income	\$ 12,795	\$ 11,328
Less:		
Direct program expense	24,679	32,048
Personnel expense	15,323	19,343
Stock-based compensation expense	13,072	13,088
Other segment items (a)	9,309	13,711
Segment net loss	\$ (49,588)	\$ (66,862)
Adjustments for reconciling items		
Consolidated Net loss	\$ (49,588)	\$ (66,862)

(a) Other segment items included in Segment net loss includes professional services, consulting and other outside services expenses, depreciation expense, insurance, facilities, and other overhead items.

15. Employee Benefit Plans

The Company maintains a retirement plan, which is qualified under section 401(k) of the Code. The plan allows eligible employees to defer, at the employee's discretion, pretax compensation up to the IRS annual limits. The Company elected to make matching contributions of \$0.4 million and \$0.5 million to the plan for the years ended December 31, 2024 and 2023, respectively.

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 principal financial officer, evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2024. 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, 2024, our Chief Executive Officer and our principal 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 by, or under the supervision of, our Chief Executive Officer and principal financial officer, and effected by our board of directors, management and other personnel, 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, 2024.

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, 2024 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.

The information required by this item and not set forth below will be set forth in the sections headed Election of Directors, Executive Officers and Information Regarding the Board of Directors and Corporate Governance contained in the Proxy Statement for our 2025 annual meeting of stockholders, to be filed with the Securities and Exchange Commission on or before April 30, 2025 (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 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.

The 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 *Transactions with Related Persons and Indemnification* 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.

The 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

Exhibit Number	Description
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, 2023, filed March 19, 2024).
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 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).

10.7*	Non-Employee Director Compensation Policy of the Registrant (incorporated by reference to Exhibit 10.7 to the Registrant's Annual Report on Form 10-K for the year ended December 31, 2023, filed March 19, 2024).
10.8†‡	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).
10.9‡*	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).
10.10*	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).
10.11*	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).
10.12*	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).
10.13*	Third Amendment to Consulting Agreement, by and between the Registrant and Aseem Z. Ansari, Ph.D., dated November 9, 2023 (incorporated by reference to Exhibit 10.13 to the Registrant's Annual Report on Form 10-K for the year ended December 31, 2023, filed March 19, 2024).
10.14*	Consulting Agreement by and between the Registrant and Rodney Lappe, Ph.D., dated November 22, 2023. (incorporated by reference to Exhibit 10.13 to the Registrant's Annual Report on Form 10-K for the year ended December 31, 2023, filed March 19, 2024).
19.1	Insider Trading Policy of the Registrant.
23.1	Consent of Independent Registered Public Accounting Firm
24.1	Power of Attorney (see signature page hereto).
31.1	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.
32.1	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.
97.1	Incentive Compensation Recoupment Policy of the Registrant (incorporated by reference to Exhibit 97.1 to the Registrant's Annual Report on Form 10-K for the year ended December 31, 2023, filed March 19, 2024).
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)(iv) of Regulation S-K.

Item 16. Form 10-K Summary

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended, the Registrant has duly caused this Report to be signed on its behalf by the undersigned, thereunto duly authorized.

Design Therapeutics, Inc.

Date: March 10, 2025

By: /s/ Pratik Shah, Ph.D.
Pratik Shah, Ph.D.
President, Chief Executive Officer and
Chairperson

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Pratik Shah, Ph.D., as his or her true and lawful attorney-in-fact and agents, with the full power of substitution, for him or her and in his or her name, place or stead, in any and all capacities, to sign any and all amendments to this Annual Report on Form 10-K, and to file the same, with all exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorney-in-fact and agent, full power and authority to do and perform each and every act and thing requisite and necessary to be done in and about the premises, as fully to all intents and purposes as he or she might or could do in person, hereby ratifying and confirming all that said attorney-in-fact and agent, or his substitute, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, this Report has been signed below by the following persons on behalf of the Registrant in the capacities and on the dates indicated.

Name	Title	Date
<u>/s/ Pratik Shah, Ph.D.</u> Pratik Shah, Ph.D.	President, Chief Executive Officer and Chairperson (Principal Executive and Financial Officer)	March 10, 2025
<u>/s/ Julie Burgess</u> Julie Burgess	Chief Accounting Officer (Principal Accounting Officer)	March 10, 2025
<u>/s/ Simeon George, M.D.</u> Simeon George, M.D.	Director	March 10, 2025
<u>/s/ Rodney Lappe, Ph.D.</u> Rodney Lappe, Ph.D.	Director	March 10, 2025
<u>/s/ John Schmid</u> John Schmid	Director	March 10, 2025
<u>/s/ Arsani William, M.D.</u> Arsani William, M.D.	Director	March 10, 2025
<u>/s/ Heather Berger, Ph.D.</u> Heather Berger, Ph.D.	Director	March 10, 2025
<u>/s/ Deepa Prasad</u> Deepa Prasad	Director	March 10, 2025



Executive Officers

Pratik Shah, Ph.D. – President, Chief Executive Officer and Chairperson of the Board of Directors of Design Therapeutics, Inc. Chairperson of the board of directors of ARS Pharmaceuticals, Inc.

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

Chris Storgard, M.D. – Chief Medical Officer of Design Therapeutics, Inc.

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. – Chief Business Officer of Iolyx Therapeutics

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 & Managing Partner of SR One Capital Management, LP.